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CHANGES IN THE FUNDUS AND IN THE BLOOD PRESSURE IN THE RETINAL ARTERIES IN INCREASED INTRACRANIAL PRESSURE

PAPILLEDEMA AND OPTIC ATROPHY *

CONRAD BERENS, M.D.
HENRY T. SMITH, M.D.
AND
LEON H. CORNWALL, M.D.
NEW YORK

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* From the Department of Neurology, Columbia University, and the Department of Surgical Research, Cornell University.

* Abridgement of a paper read before the Association for Research in Nervous and Mental Disease, Dec. 29, 1927.

VALUE OF THE OPHTHALMOSCOPE IN THE DIAGNOSIS OF DISEASES OF THE NERVOUS SYSTEM

The great value of the ophthalmoscope in the study of diseases of the nervous system was first appreciated by von Graefe, about the year 1859, and at practically the same time by Businelli of Rome. These observers noted papilledema in its relation to brain tumor—now recognized as a physical sign of great importance. The recent invention of the ophthalmodynamometer by Bailliart [1] has provided an additional diagnostic refinement by which it may often be possible to detect increased intracranial pressure before choked disk develops, or before other signs of increased pressure can be determined with the ophthalmoscope.

CHANGES IN THE FUNDUS

In many cases the symptoms of increased intracranial pressure are slight, and the swelling of the disk may even precede headache, so that the earliest fundus changes, namely, hyperemia and edema (Knapp), or congestion with edema (Gowers) may not be in evidence. The upper or lower margins of the disk are usually the first to be blurred, this change then extending to the nasal side. Yet the physiologic variations in the size of the blood vessels, the color of the nerve head and the appearance of the nerve margins are so numerous that it is often impossible definitely to postulate the increased intracranial pressure from ophthalmoscopic examination alone, unless previous periodic examinations of the fundi have been made. It is important to realize that greatly increased intracranial pressure may not give ophthalmoscopic signs, with the exception of those which may be detected by the use of the ophthalmodynamometer and by a comparative study of the diastolic pressure in the retinal and brachial arteries.

Slight fulness of the veins is likely to be the first vascular change detected; this suggests interference with the return circulation. At times increased tortuosity may then be noted. Venous pulsation not previously in evidence may now be observed, but ordinarily changes will not be detected in the arteries. Slight clouding of the circumpapillary area of the retina can at times be made out, but it is seldom that any appreciable swelling of the disk can be determined. In certain cases, however, the disk will become edematous before hyperemia is noted. Swelling of the disk may be rapid, progressing to its maximum within a few days. Again, a swelling of no more than from ½ to 2 diopters may persist for weeks or months, without producing permanent visual disturbance. This is illustrated in the following cases:

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1. Bailliart, P.: La circulation rétinienne dans les états d'hypertension intracranienne, Ann. d'ocul. **159**:785, 1922.

REPORT OF CASES

CASE 1.—G. C. D., a woman, aged 51, was seen in consultation by Dr. Harvey Cushing. She presented chronic interstitial nephritis, apical dental infections, possible sinus infection, evidences of pituitary tumor by two roentgenograms and other signs of brain tumor, or arachnoiditis. A unilateral papilledema had persisted for two years without loss of vision, but was not improved by extraction of the infected teeth, nasal treatment, spinal puncture or drugs. Some improvement was noted after the administration of mixed catarrhal vaccines, but it was impossible to determine whether this was due to the effect of nonspecific protein,

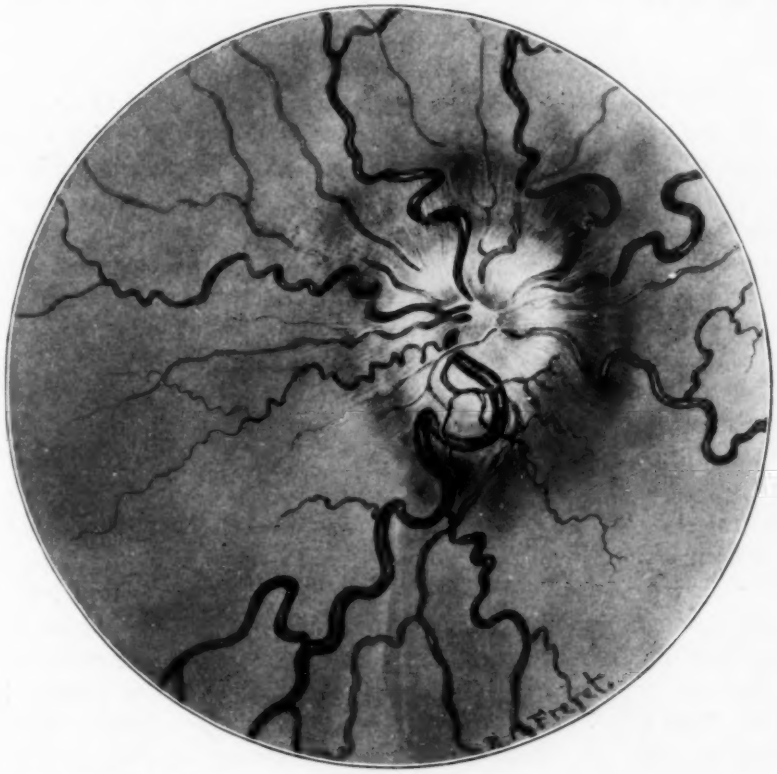

Fig. 1.—Papilledema of 3 diopters in a patient with increased pressure of the cerebrospinal fluid, equalling 480 mm. of water at the time of drawing.

to the specific effect on bacteria in nasal sinuses or to some undiscovered infective focus, or whether this was merely a coincidence, the patient perhaps actually presenting a brain tumor which would give trouble later. The difficulties in diagnosis offered by even a unilateral papilledema are well illustrated by this case, showing how often operation may be done too early or, how with patience and careful observation, operation may eventually prove unnecessary. After two years this woman has 20/15 vision in each eye and normal visual fields. If, in the absence of localizing signs the ophthalmologist suggests decompressive measures, his decision must be based on close observation of the vision, with quantitative studies of the visual field, of the fundi and of the retinal blood pressure.

CASE 2.—E. T., a woman, aged 36, presented bilateral papilledema of from 3 to 3½ diopters, which had persisted for nine months (fig. 1). In neither eye did the visual acuity decrease below 20/30. Apical dental infection and chronic ethmoiditis were also present. The hemorrhages and exudates led two consulting ophthalmologists to believe that the patient's condition had been brought about by some toxic factor, rather than by the existence of a brain tumor. Yet elimination of the infective foci did not have any effect on the papilledema, although the hemorrhages became less numerous and finally ceased entirely. Retinal diastolic pressure was at first high —60 mm. of mercury—nearly equaling the brachial diastolic pressure of 70, but it later fell to 35 mm. of mercury, although the spinal fluid pressure was 480 mm. of water.

INCREASED INTRACRANIAL PRESSURE

Ocular Symptoms.—These cases show that visual acuity may remain unaffected even when papilledema is of long standing, and that without the use of the ophthalmoscope, other signs or symptoms of papilledema cannot be discovered. When visual acuity is affected, the onset is usually gradual, the earliest complaint being of blurring of vision at intervals. These attacks may take place several days apart, but in the second case just cited there were from seven to fifteen attacks every day for a period of several months. Later, the blurring of vision may become more severe, lasting from fifteen to twenty minutes at a time, during which the patient may become almost totally blind, though vision usually returns rapidly.

Papilledema may persist for years, but usually the swelling will begin to subside within a few weeks. Improvement, however, is not always progressive, as exacerbations of the symptoms—including papilledema—may recur at intervals. As the swelling subsides the color of the disk generally changes to a more grayish hue, and its outlines become more pronounced. If the radially arranged striae have been prominent, they disappear as the congestion of the veins decreases and the arteries become more visible. Even when the acute process has abated, there may be slight elevations of the disk, frequently ½ diopter, and its margins are usually indistinct. A characteristic gray pallor will overspread the disk, although the veins may still be somewhat engorged and tortuous. Atrophy of the nerve commonly results, due to compression of the nerve fibers, but vision is seldom completely lost.

One patient who came under our observation showed swelling of the nerve amounting to 3 diopters; yet this subsided without leaving demonstrable ophthalmoscopic evidence of its previous existence. In this particular case the cause of the papilledema was never definitely determined.

If the intracranial pressure is lowered by operative measures, the edema may subside rapidly, even though cure of the underlying disease is not brought about. Vision may be conserved if it has not been

seriously disturbed, and further compression of the nerve can be avoided. One of our patients who previously had light perception only, was able to read large print two days after operation, the edema of the nerve having subsided rapidly the very day the intervention was undertaken.

Pathologic Changes.—The microscopic changes which produce the ophthalmoscopic signs of increased intracranial pressure have engaged the attention of many students of ophthalmology.[2] Pathologically con-

Fig. 2.—Optic nerve, showing edema, in a case of metastatic sarcoma of the brain.

sidered, simple edema appears to be the factor of most importance, the fluid contained in the tissues serving to obliterate the physiologic cup by swelling of the disk, to separate the nerve fibers so as to form folds which appear as fine striations concentric with the margins of the disk, to cause a dispersion of light which blurs the disk and the surrounding

2. Parsons, J. H.: Pathology of the Eye, New York, G. P. Putnam's Sons, 1908, vol. 4, p. 1349. Paton, L., and Holmes, G.: Pathology of Papilledema; A Histologic Study of Sixty Eyes, Brain **33**:389, 1911.

retina, and finally to narrow the lumen of the arteries of the disk by direct compression, thus adding to the engorgement and tortuosity of the veins by retarding the return circulation. There are few signs of inflammation of the optic nerve, but when the condition has persisted for a long time, round cell infiltration may be noted within the walls of the vessel. The nerve fibers may also undergo degeneration, breaking up into masses, the so-called cytoid bodies, which, according to Parsons, undergo lipoid degeneration and ultimate absorption. These products

Fig. 3.—Optic nerve, in so-called retinitis of nephritis. The edema and hemorrhages in the nerve head are clearly visible; the distention of the dural sheath of the optic nerve and the absence of inflammatory signs may be noted.

of degeneration of the nerve fiber are supposed by some authors to be the sole cause of the white areas observed around the disk, but we have seen them appear early at the time the hemorrhages were first noted, disappearing as the hemorrhages were absorbed. Some of these, at least, we believe to have been due to exudates.

Through the courtesy of Dr. William V. Cone of the Presbyterian Hospital, histologic examinations have been made of the optic nerves in

a case of uncomplicated brain tumor, in one of so-called retinitis of nephritis and in a patient suffering from an abscess of the temporal lobe complicated by streptococcic meningitis. The intra-ocular division of the optic nerves showed papilledema clinically and microscopically. In each case the area immediately overlying the entrance to the optic nerve exhibited the same type of swelling of tissues without inflammatory signs. The arteries of the retina and choroid had undergone advanced angiosclerotic changes in the patient with renal retinitis, and there were

Fig. 4.—Optic nerve, showing edema of nerve in patient with brain abscess and meningitis. Inflammatory changes are not in evidence in the intra-ocular division of the nerve, although there is inflammation of the leptomeninges.

hemorrhages and exudates in the retina, and hemorrhages in the intra-ocular division of the optic nerve. The retina of the patient with meningitis was normal, but there were marked signs of perineuritis with lymphocytic infiltration of the leptomeninges. In these three cases the picture in the intra-ocular division of the nerve was that of infiltration of tissue with noninflammatory fluid, the cause of which one would naturally suppose to be the same in each case (figs. 2, 3 and 4).

PAPILLEDEMA AND OPTIC ATROPHY

Pathogenesis of Papilledema.—The picture presented by these nerves, the rapid development and subsidence of papilledema clinically and experimentally, and the observation of Parker [3] that the edema of the nerve head is usually greater in the eye with the lower tension would lead to the belief that mechanical increase in pressure of the cerebrospinal fluid is the most important single factor in the production of papilledema. Experiments on injections in animals conducted under the direction of Dr. J. E. Sweet, of the Department of Surgical Research, Cornell University (fig. 5), as well as those reported by Gifford [4] and Wegefarth,[5] have convinced us that there is lymphatic drainage from the eyeball along the central vessels, and it is our belief that blocking of this drainage is an important factor in the production of the edema. In some cases toxic products may be formed which tend to close these lymph channels, producing edema of the optic nerve, but it is the final blocking of the lymphatics by atrophy from pressure which may account for the late appearance of papilledema in some of the cases of brain tumor. In the majority of instances there will be no increase in the intra-ocular pressure, as this is regulated by the choroidal circulation through the vortex veins, and by the escape of aqueous through the canal of Schlemm. Is it not possible that the absence of papilledema in some cases in which the intracranial pressure is known to be high may be accounted for by absence of this blocking of lymphatic drainage? Hydrocephalus in children frequently offers such a problem.

In our opinion, increased pressure in the sheath, if it rises acutely, may block lymphatic drainage from the vitreous, retina and intra-ocular division of the optic nerve, thus bringing about papilledema. If the increase in pressure is slow, the process being chronic in nature, there will be readjustment of the circulation to meet the changing conditions, and papilledema will not be produced. Later, in chronically increased intracranial pressure from brain tumors and similar causes, pressure atrophy may close the lymphatics, or toxic products of cell destruction may produce enough inflammation to block lymphatic drainage more completely. There is no doubt that venous stasis can exist in the branches of the central veins of the retina, even though there is free anastomosis of the central vein with the veins from the orbit which do not empty into the cavernous sinus. Even though the pressure in the central vein does not appear to be raised in the presence of papilledema,

3. Parker, W. R.: Relation of Choked Disk to the Tension of the Eyeball, J. A. M. A. **67**:1053 (Oct. 7) 1916.

4. Gifford, Harold: Further Experiments on the Lymph Streams and Lymph Channels of the Eye, Arch. Ophth. **21**:171, 1892.

5. Wegefarth, Paul: Studies on Cerebrospinal Fluid. V. The Drainage of Intra-Ocular Fluids, J. M. Research **31**:119, 1914.

as studied by the Bailliart method, hemorrhages and exudates may be explained, even in the absence of increased intra-ocular pressure, by the presence of some slight obstruction to circulation. We believe that this blocking of lymphatic drainage is a far more important factor in producing the edema than is venous engorgement.

Fig. 5.—Section of the optic nerve of a cat. Eye enucleated three days after injection of 5 minims of trypan blue into the vitreous chamber. Staining of the lymphatics around the central vessels and absence of the stain in the surrounding nerve fibers should be noted.

Differential Diagnosis.—It is important in the early stages of swelling to differentiate between papilledema, papillitis and pseudopapillitis, a diagnostic feat which will usually tax all the resources of the ophthalmologist and neurologist. We are familiar with the fact that the eye in

which papillitis exists will have the vision diminished early, and out of proportion to the degree of swelling present, as this rarely exceeds from 1 to 3 diopters. This is especially true if the papillomacular bundle is affected, for, as we have already seen, the patient with papilledema may retain practically unaffected vision for months or even years. The blood vessels in papilledema frequently show marked disturbance; the veins appear tortuous, and the arteries are usually narrow. In papillitis, on the other hand, the arteries may be normal in size, showing early evidence of perivasculitis, while the size of the veins will be only slightly diminished.

Enlargement of the Blind Spot.—In papilledema, enlargement of the blind spot will not be so extensive as in papillitis, nor will it be in proportion to the degree of nerve swelling. The difference may be easily understood when one considers that in the first instance the enlargement is frequently only a mechanical condition, caused by the spreading aside of the rods and cones at the entrance to the optic nerve in the eyeball. In papillitis, the enlargement is due to the depressed function of the nerves themselves, resulting from the action of some poison. Study of the blind spot is extremely important in differentiating pseudopapillitis from true papillitis and papilledema, for in pseudoneuritis the blind spot is extremely small.

Excluding diseases such as myopia, medullated nerve fibers and papilledema, all of which are easily diagnosed with the ophthalmoscope, in our experience, the most common cause of enlargement of the blind spot has been infection in the posterior ethmoid and sphenoid sinuses. It must not be forgotten that glaucoma without characteristic cupping of the optic nerve can simulate sinusitis with involvement of that nerve, for besides enlargement of the blind spot it has five symptoms in common: paracentral and central scotomas, sluggish reaction of the irides with dilated pupils, blurring of distant vision and failure of accommodation. Quantitative perimetry and tonometry give valuable differential diagnostic points.

Another important diagnostic point is the disproportionate increase in the retinal diastolic blood pressure over the brachial diastolic pressure. This is of more importance in early attempts to establish the diagnosis, for, as has been previously noted, when edema is fully developed the retinal pressure is likely to fall.

CONDITIONS PRODUCING PAPILLEDEMA AND CHANGES IN THE FUNDUS

In the differential etiologic diagnosis from symptoms of the eye and signs of increased intracranial pressure, numerous conditions have been noted in ophthalmologic literature as productive of the manifestations

which we are considering. It will suffice to mention a few especially characteristic instances coming within our own experience.

Brain Abscess.—Papilledema is frequently seen in brain abscess. In the experience of one of us (C. B.) papilledema, unilateral or greater in one disk, if seen early in the disease, suggests the possible localization of the abscess on this side. The presence of unilateral papilledema, however, should not be considered of great diagnostic importance unless the tension of the eyes is equal or greater on the side of the more pronounced edema.

Sinusitis.—Papilledema is not characteristic of involvement of the optic nerve due to sinus disease, but the differential diagnosis may be difficult. Although unilateral choked disk is usually seen in diseases of the accessory sinuses, particularly the posterior ethmoids and sphenoids, and in diseases of the orbit such as abscesses and tumors, it should be remembered that infections and tumors may also extend from the middle cranial fossa into the orbit. One of us (C. B.) has seen one patient with unilateral papillitis which was apparently due to apical dental infection, and Langdon [6] has reported his observations in a similar case wherein the cause was an infective focus in the tonsils. As has already been stated, the nerves seem most often to be involved in posterior ethmoiditis and sphenoiditis, for we have seen only two patients in whom enlargement of the blind spot was apparently caused by infection in sinuses other than the ethmoid and sphenoid. One patient had frontal sinusitis and the other inflammation of the antrum of Highmore, and pus was present under pressure in both instances.

Arteriosclerosis.—Arteriosclerotic neuroretinitis may closely simulate retinitis of renal origin, and in some cases sufficient edema of the optic nerve is present to make one suspicious of increased intracranial pressure. The marked sclerosis of the retinal vessels usually leads to a correct diagnosis, although arteriosclerosis has been present in the eyes of all patients suffering from renal retinitis whom we have examined microscopically. Naturally the existence of arteriosclerosis does not exclude an intracranial lesion and an increase in intracranial pressure. It is our belief that the arteriosclerosis and the nephritis may have a common origin, as so-called renal retinitis has been seen when kidney lesions could not be demonstrated and when the arteries were not sclerosed, while albumin and casts have been found in the urine of patients presenting so-called arteriosclerotic neuroretinitis. We have frequently observed those conditions associated with focal infections,

6. Langdon, H. M.: Unilateral Papillitis Apparently Due to Infected Tonsils, Am. J. Ophth. **6**:495, 1923.

particularly when streptococci were the organisms concerned, and here it was the teeth, tonsils and nasal sinuses which came most persistently under suspicion.

Optic atrophy may be the final outcome, caused by destruction and failure of the blood supply, and probably likewise by the action of toxins on the cells of the retina. Atrophy may also result from pressure of the sclerosed intracranial arteries, especially the internal carotids, on the optic nerves or chiasm.

Epidemic Encephalitis.—Although paralysis of the ocular nerves is common, involvement of the intra-ocular portion of the optic nerve seldom occurs in epidemic encephalitis. Papilledema is rarely seen and has never come under our personal observation. The optic nerve was involved in three of sixteen cases of epidemic encephalitis which we saw at the Vanderbilt Clinic. Neuritis of the intra-ocular portion of the nerve was present in one and retrobulbar neuritis in two cases.

DIAGNOSIS OF INCREASED INTRACRANIAL PRESSURE IN THE ABSENCE OF PAPILLEDEMA THROUGH STUDY OF THE RETINAL BLOOD PRESSURE

We are indebted to Bailliart [1] for a method of detecting intracranial hypertension in serous meningitis through study of the retinal blood pressure. As he has quaintly expressed it: "The retina is the image of the brain and the retinal circulation the daughter of the cerebral circulation." The retina is embryologically the direct extension of the forebrain, the retinal arteries are derived from cerebral arteries and the veins return to the cranial cavity. The arteries of the retina resemble cerebral arteries in that they do not anastomose freely, and because they are ordinarily under an even constant pressure. It is thus readily understood why retinal pressure seems to vary with changes in intracranial pressure which undoubtedly influence cerebral arterial pressure, even though we are still in ignorance of the precise mechanism by which this is brought about.

RELATION OF THE RETINAL TO THE CEREBRAL CIRCULATION

Two theories have been advanced to explain the changes in the retinal blood pressure observable when intracranial pressure is increased: The mechanical theory considers the cerebral arterial hypertension and the increased diastolic pressure in the retinal arteries a passive condition due to mechanical obstruction of the cerebral veins, brought about by distention of the ventricular and subarachnoid systems. The vasomotor theory views the hypertension as an active condition due to vasomotor influences. Neither of these theories adequately explains all

the known facts. From our own studies we have learned that the increase in cerebral venous pressure by jugular compression is accompanied by an increase in the retinal diastolic pressure, *pari passu* with the rise in the cerebrospinal fluid pressure. The observations of others as well as our own experience have convinced us that arterial hypertension is not always general, but may be localized in the brain. In this connection it is interesting to note that in glaucoma, in which the

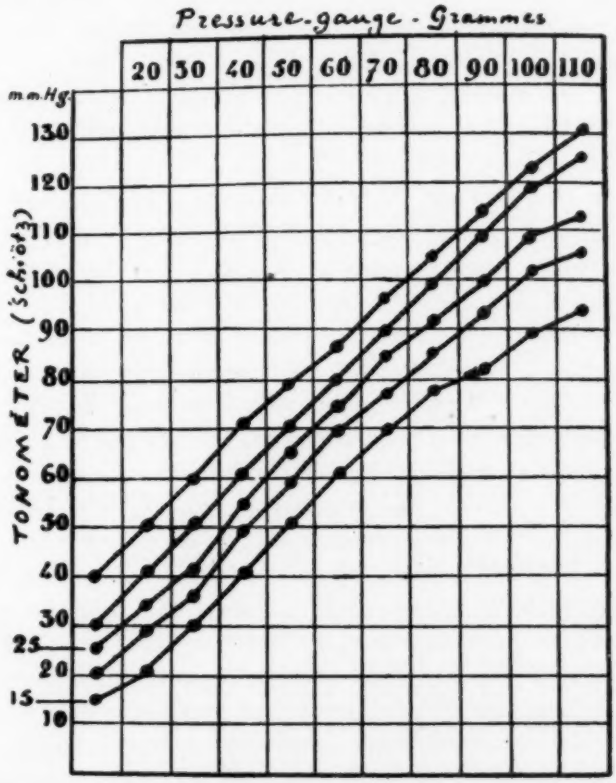

Fig. 6.—Chart arranged by Magitot and Bailliart for determining the retinal blood pressure in millimeters of mercury.

intra-ocular pressure is raised and the diastolic, systolic and venous pressure in the retina extremely high, many patients do not show abnormal increase in the brachial blood pressure.

BAILLIART'S METHOD OF DETERMINING BLOOD PRESSURE IN THE CENTRAL RETINAL ARTERY

For the details of Bailliart's method, and its modifications and applications by Magitot, the reader is referred to the publications of these

investigators.[7] In table 1 will be seen the observations in a study of the cerebrospinal fluid pressure as compared with the retinal diastolic and brachial pressure, which were made in the Department of Neurology, Columbia University. These results have convinced us of the value of the Bailliart method in certain cases for studying changes in the pressure of the cerebrospinal fluid, and for detecting increased intracranial pressure in the absence of papilledema. While we fully appreciate that any method of studying retinal blood pressure, which includes pressure on the eyeball, is bound to involve inaccuracies, we are still of the opinion that a trained observer, using tested instruments over a period of a few months, will be able to obtain valuable clinical data, particularly if he is in a position to make continuous study of the patients from one day to another.

Summary of Table of Cases· Comparison of Pressure in the Retinal and Brachial Arteries and in the Spinal Fluid.—In six of eight patients examined a simultaneous study was made of the diastolic pressure in the retinal and brachial arteries, and of the spinal fluid pressure as recorded in millimeters of mercury before and after withdrawal of a measured amount of spinal fluid. This study brought to light the fact that five of these six persons had a disproportionate increase in the retinal diastolic pressure as compared with the brachial diastolic pressure. All five also showed increased intraspinal pressure as recorded by the mercurial manometer. The one patient (case 3), who had normal diastolic retinal and brachial pressure, had a normal pressure of the spinal fluid as well. It appears from consideration of these controlled studies of retinal blood pressure, as compared with brachial pressure and manometric studies of cerebrospinal fluid pressure, that the ophthalmodynamometer of Bailliart gives strongly suggestive evidence of the presence of increased intracranial pressure in the absence of papilledema, disease of the retinal arteries and general arterial hypertension.

Pressure of the Cerebrospinal Fluid After Spinal Puncture.—In Kalt's[8] studies of the retinal blood pressure after spinal puncture, a fall

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7. Bailliart (footnote 1): La circulation rétinienne, particulièrement dans ces rapports avec la circulation cérébrale, Rev. méd. de la Suisse Rom. **45**:129, 1925. Magitot, A. P.: How to Know the Blood Pressure in the Vessels of the Retina, Am. J. Ophth. **5**:777, 1922. Bailliart, P.: Recherches sur la pression artérielle dans les branches intra-oculaires, Ann. de méd. **4**:329, 1917; La pression artérielle dans les branches de l'artére centrale de la rétine; nouvelle technique pour la déterminer, Ann. d'ocul. **154**:648, 1917; L'état actuel de nos connaissances sur la pression artérielle rétinienne, ibid. **157**:308, 1920.

8. Kalt, M.: Pression artérielle rétinienne dans l'hypertension intracranienne, L'expansion scientifique Française, 1927.

TABLE 1.—*Comparison of the Pressure in the Retinal Arteries, Brachial Arteries and Spinal Fluid*

Case	Name	Age	Diagnosis	Date	Time of Examination or Spinal Puncture	Brachial Blood Pressure with Patient Sitting		Tension with Bailliart Corneal Tonometer		Retinal Blood Pressure				Spinal Pressure; Amount Withdrawn; Reinjection Pressure	Comment
										Right Eye		Left Eye			
						Systolic	Diastolic	Right Eye	Left Eye	Systolic	Diastolic	Systolic	Diastolic		
3	E. H.	..	.....	4/ 4/27	4:15 p.m.	111	65	.....	.....	4:20 p.m. ...	... 29	...	...	7-8 mm. of mercury after withdrawal pressure was 4 mm. of mercury	Brain tumor (?); optic atrophy retrobulbar each eye
										after puncture, 5:00 p.m. ...	38				
				4/13/27	.....	102	70	17 B. C.*	17 B. C.	...	32	...	34	.....	Slight headache following puncture
4	M. B.	..	Hemianopia, brain tumor	4/ 4/27	4:45 p.m.	165	75	19 B. C.	19 B. C.	...	40	...	42	Spinal fluid pressure 15 mm. of mercury; after withdrawal of 12 cc. pressure was 2 mm. of mercury; after injection of 25 cc. of arsphenaminized serum, pressure 24	4/14/27, has had headache since puncture, not influenced by posture, refused reexamination
										4:50 p.m. ...	44	...	50		
										5:00 p.m. ...	40	...	40		
5	J. B.	61	Neurosyphilis	4/20/27	4:35 p.m.	132	64	18 B. C.	17 B. C.	130	50	130	52	9 mm. of mercury; after withdrawal of 12 cc. pressure was 5 mm. of mercury	Cataract, hard to see vessels
										4:50 p.m. 130	65	4:50 p.m. 130	58		
				4/27/27	.....	118	64	14 B. C.	14 B. C.	71	37	71	37	.....	No headache following puncture 1 week
6	A. S.	..	Tabes dorsalis	4/ 4/27	4:20 p.m. spinal puncture	120	78	18 B. C.	18 B. C.	...	70	...	70	Pressure 12 mm. of mercury; after fluid withdrawal pressure 4 mm. of mercury; Wassermann 4+; cell .50; colloidal gold 5433210 0	Headaches second day after puncture lasted 2 days then felt well, refused examination of retinal pressure 1 week after puncture
					4:40 p.m. examination	118	78	.....	.....	...	83	...	83		
7	M. F.	42	Cerebrospinal syphilis	5/ 1/27	4:50 p.m.	120	78	15 B. C.	15 B. C.	85	48	95	48	12 mm. of mercury; after 25 cc. withdrawn pressure was 2 mm. of mercury	
					5:04 p.m.	...	..	.....	.....	92	55	85	62		
8	I. P.	47	.....	.....	4:30 p.m.	105	58	23 B. C.	21 B. C.	92	36	...	...	Slight increase in pressure, 24 cc. removed, 20 cc. arsphenaminized serum injected	
					4:45 p.m.	...	..	.....	.....	...	46				
	E. K.	40	Papilledema	3/17/27	.....	150	120	18 B. C.	18 B. C.	100	65	130	80		
9	A. B.	50	Optic atrophy	4/17/27	.....	140	90	21 B. C.	21 B. C.	125	55	130	65	12 mm. of mercury; after 20 cc. withdrawn pressure was 4 mm. of mercury	No headache or nausea following puncture

* B. C. indicates Bailliart corneal.

in pressure was noted in six of eight cases. Bailliart, however, found the pressure higher after spinal puncture. In cases 7, 8 and 9 recorded in table 1, the pressure in the retinal arteries was higher after spinal puncture than it was before. In case 4, however, it was lower, although 25 cc. of arsphenaminized serum was injected, and immediately following this injection the pressure of the spinal fluid was 24 mm. of mercury. This apparent discrepancy may be explained by the local increase in the cerebrospinal fluid pressure. In case 8, wherein the pressure was higher after spinal puncture, 20 cc. of arsphenaminized serum was injected.

If the increased retinal diastolic pressure actually signifies increased intracranial pressure immediately following spinal puncture, might not this be due to rapid dilatation of the previously compressed cerebral vessels and rapid formation of spinal fluid? One is accustomed to see rapid formation of the aqueous humor after paracentesis has been performed. If the puncture wound remained open, or if there was marked sclerosis of the cerebral vessels or impairment of the secretory function, an explanation might be provided for the fact that cerebrospinal fluid pressure was not raised at all in some of the patients on whom spinal puncture was made.

Ascertaining the Effect of Treatment.—That a study of the retinal blood pressure may also give valuable data concerning the effect of treatment on the pressure of the cerebrospinal fluid, as well as on the progress in the condition, is suggested by a study of table 2.

In cases 10 and 11 there was a pathologic increase in diastolic pressure in the retinal arteries as compared with the brachial arteries; this suggested brain tumor. Spinal puncture apparently caused a decrease in the pressure of the cerebrospinal fluid in case 11. Intravenous injection of a 20 per cent solution of dextrose did not seem to have any immediate effect in lowering the retinal blood pressure in case 10, though the vertigo from which the patient was suffering appeared to be somewhat relieved by the injection. The patient in case 12 had a bilateral papillitis of 3 diopters, but the retinal diastolic pressure was not elevated in comparison with the brachial diastolic pressure. At operation on the ethmoids of this patient pus was found, and the case had a fatal termination. Our observations are in accordance with those of Kalt, that when papilledema has developed one third of the patients will show normal blood pressure in the retinal arteries, while in many others the pressure will be only slightly elevated. We are also able to confirm Kalt's observation that some patients with papilledema show variations of the pressure in the retinal arteries. Case 11 in table 2 is an example of this. In the patients in cases 11 and 12 there was low pressure in the retinal arteries when papilledema had become well established.

TABLE 2.—*Retinal Blood Pressure in Suspected Intracranial Disease*

Case	Name	Age	Diagnosis	Date	Time of Examination or Spinal Puncture	Brachial Blood Pressure with Patient Sitting		Intra-ocular Tension		Blood Pressure Ocular Artery		Spinal Pressure; Amount Withdrawn; Reinjection Pressure	Comment
						Systolic	Diastolic	Right Eye	Left Eye	Right Eye, Diastolic	Left Eye, Diastolic		
10	F. Y. D.	..	.....	3/17/27	.....	135	120	.....	.....	.....	88	.....	Question of pons tumor, bilateral ethmoiditis, advanced angiosclerosis, hemorrhages from retina, chronic nephritis
				4/28/27	.....	220	123	21 B. C.	20 B. C.	.....	120		
				5/ 4/27	6:00 p.m.	218	120	.....	.....	.....	81	200 cc 20% dextrose injected intravenously	
					6:35 p.m.	...	...	.....	.....	.....	81	.....	No change in retinal diastolic pressure 30 minutes after dextrose; patient died during second attack of pneumonia in 6 months
11	E. T.	36	Papilledema each eye, R. 3.5 D., L. 3 D.	1/26/27	.....	118	82	17 B. C.	17 B. C.	87/37	92/35	.....	Recurring attacks of blurred vision, no headache, bilateral choked disks, question of brain tumor but neurologic examination negative
			3½ each eye	3/26/27	.....	118	82	22 B. C.	18 B. C.	45	60		
				3/31/27	.....	108	78	17 B. C.	20 B. C.	48	52		
				4/ 7/27	.....	112	70	20 B. C.	17 B. C.	60	57		
				4/14/27	.....	116	70	19 B. C.	19 B. C.	42	43	25 cc. under pressure, not measured by manometer	
			R. ½ D., L. 2 D.	4/19/27	.....	120	78	16 B. C.	19 B. C.	52	50	.....	Headaches following puncture beginning to improve, attacks of blurred vision less frequent, no headaches
				4/28 27	.....	114	80	21 B. C.	2[illegible] B. C.	65/55	70/32		
12	E. T.	..	Purulent bilateral ethmoid, bilateral papilledema, R. 3.5 D., L. 3 D.	1/26/27	.....	118	82	17 B. C.	17 B. C.	85/38	87/40	.....	X-ray of head showed chronic ethmoiditis, temperature 104, pus in both ethmoids; died during radical operation on ethmoids

RETINAL BLOOD PRESSURE IN HEALTHY SUBJECTS

Using the Bailliart technic, eleven persons between the ages of 15 and 39 years, with an average age of 28.4 years, were examined in the sitting position to determine the systolic and diastolic pressure in the retinal arteries. The brachial blood pressure of the group averaged 118/76 in millimeters of mercury. Intra-ocular tension, as studied by the Bailliart corneal tonometer averaged 17.5 in the right eye, and 17 in the left eye. The retinal pressure averaged 68.2/32.3 in millimeters of mercury on the right and 67.4/32.2 in millimeters of mercury on the left.

TABLE 3.—*Normal Pressure in the Retinal Arteries in Sitting Position*

Assisted by Dr. Henry T. Smith

Case	Name of Patient	Age	Method	General Blood Pressure		Ocular Tension, Bailliart Tonometer		Retinal Blood Pressure			
								Diastolic, Mm. of Mercury		Systolic, Mm. of Mercury	
				Systolic	Diastolic	R. E.	L. E.	R. E.	L. E.	R. E.	L. E.
1	A. H.	28	Bailliart	118	84	17	17	38	38	80	76
2	H. S.	20	Bailliart	114	80	20	18	45	38	88	78
3	M. K.	39	Bailliart	124	90	18	18	42	48	84	82
4	R. D.	24	Bailliart	110	60	16	16	30	25	58	55
5	E. S.	30	Bailliart	124	75	18	16	30	30	72	72
6	E. G.	31	Bailliart	130	86	17	17	32	34	70	72
7	B. S.	29	Bailliart	116	85	18	18	30	30	72	74
8	G. W. K.	34	Bailliart	126	78	16	18	34	38	68	74
9	W. E. S. G.	15	Bailliart	102	55	18	16	18	18	36	36
10	R. M. C.	32	Bailliart	114	70	17	17	25	25	58	58
11	T. P. C.	30	Bailliart	124	80	18	18	30	30	64	64
Low		15	Bailliart	102	55	16	16	18	18	36	36
High		39	in each	130	90	20	18	45	48	88	82
Average		28.4	case	118	76	17.5	17	32.2	32.2	68.2	67.4

These figures are lower than those obtained by other observers, but this is in a measure offset by the fact that the persons in our group were healthy young adults chosen at random, none of them having serious defects of the eye, although two complained of headache. The study was made when we had had a year's experience with the Bailliart method; the readings at first were much higher and probably less accurate. In order to determine the effect of posture and jugular compression on retinal blood pressure, several patients were studied while standing, sitting and lying prone, the spinal puncture needle being inserted when jugular compression was made. A fairly typical reaction is recorded in table 4. It may be seen from the data recorded in this table that retinal diastolic pressure increases when the patient lies down, although in the persons examined the brachial diastolic pressure has been found lower. Jugular compression in the four patients so far studied has always been accompanied by a marked rise in the pressure of the cerebrospinal fluid, and a marked and apparently immediate increase in the diastolic pressure in the retinal arteries. The diastolic

pressure in the central retinal arteries of eight patients, examined by the Bailliart method averaged 35 mm. of mercury standing, and 41 mm. of mercury lying prone; in all but one case—in which there was no apparent change in the pressure—the figures were higher in patients who were reclining.

COMPARISON WITH OBSERVATIONS OF OTHER INVESTIGATORS

The average diastolic and systolic pressure in the intra-ocular arteries as given by several other authors using various technics, is 48.3 diastolic, and 87.7 systolic in millimeters of mercury. The average of several authors using Bailliart's method is 43 diastolic and 78.3 systolic in milli-

TABLE 4.—*Effect of Jugular Compression and Posture on Retinal Blood Pressure*

Name, Age, Date, Diagnosis	Time, p.m.	Brachial Blood Pressure, with Patient Lying		Intra-ocular Pressure, Bailliart Method, with Patient Lying		Blood Pressure, Central Artery Retinal, with Patient Lying		Spinal Fluid Pressure, Mm. of Mercury, Patient Lying on Side	Comment
		Systolic	Diastolic	R. E.	L. E.	R. E.	L. E.		
U. C.	5:00	112	65	17	17	83/43	83/43	..	Before puncture, patient sitting
39	5:10	...	..	..	..	/63	.....	..	Lying prior to insert
	5:15	...	.	..	..	/65	.....	20	After insertion needle
10/27/27	5:25	...	..	..	..	/80+	.....	70	Jugular compression 15 seconds
Cerebrospinal syphilis	5:27	...	..	..	..	/90	.....	75	Jugular compression 15 seconds
	5:28	...	..	..	..	...	.....	8	Removal 25 cc.
	5:30	...	..	..	..	...	.....	6	Removal 30 cc.
	5:32	...	..	..	..	...	.....	4	Removal 35 cc.
	5:36	...	..	..	..	/65	.....	..	After withdrawal of needle

meters of mercury; with Seidel's [9] method 45.6 diastolic and 95 systolic in millimeters of mercury. As in practically all instances the blood pressure, the position of the subject and his age are not recorded, it is somewhat difficult to make a just comparison between these figures and our own. In general it may be said, from the experimental and clinical data which we have been able to obtain by the use of Bailliart's ophthalmodynamometer, that in the absence of papilledema, disease of the retinal arteries and general arterial hypertension, a diastolic blood pressure in the central artery of the retina greater by 10 to 15 mm. of mercury than one-half the brachial diastolic blood pressure, when the patient is sitting or standing, strongly suggests increased pressure in the cerebral arteries, the result of increased intracranial pressure. The exact mechanism which produces this phenomenon, however, is not definitely determined.

9. Seidel, Erich: Zur Blutzirkulation im Ziliargefässsystem, Ber. ü. d. Versamml. d. ophth. Gesellsch. **44**:79, 1924.

VALUE OF DETERMINING RETINAL BLOOD PRESSURE IN BRAIN TUMOR

Spinal puncture is conceded to be dangerous in the presence of brain tumor, and the procedure sometimes substituted for it—combined lumbar and ventricular puncture, or puncture of the lateral ventricles—is a major surgical operation. Therefore, if a brain tumor is suspected, study of the retinal blood pressure is apparently of practical value in determining the presence or absence of increased intracranial pressure, as well as for noting changes of pressure occurring in the absence of papilledema.

CONCLUSIONS

1. The ophthalmoscope and the ophthalmodynamometer of Bailliart are valuable diagnostic aids in the diagnosis of diseases of the nervous system.

2. Changes in the fundus, if properly interpreted, give valuable information when increased intracranial pressure is suspected. Negative observations, unless the retinal blood pressure is also known, are not of great importance.

3. Papilledema is frequently a late, rather than an early, sign of increased intracranial pressure, and may be absent in the presence of hypertension of long standing.

4. From clinical, pathologic and experimental studies of the pathogenesis of papilledema, the most important factors in its production appear to be mechanical blocking of the lymphatic drainage by pressure of the cerebrospinal fluid on the optic nerve and the lymphatic channels which surround the central artery of the retina. Mechanical obstruction to venous outflow is possibly a less important factor in the production of hemorrhages and exudates.

5. When papilledema is established, the observations on the retinal blood pressure may be so misleading as to indicate a low intracranial pressure in certain cases when the intracranial pressure actually is high. An explanation is not offered for this phenomenon.

6. From the standpoint of pathologic changes, simple edema seems to be the most important single factor in the production of the microscopic and ophthalmoscopic picture of papilledema in brain tumor, meningitis and the so-called retinitis of nephritis.

7. Bailliart's method for determining the diastolic and systolic blood pressure in the central artery of the retina is valuable to the trained observer in spite of inaccuracies. The authors' observations for a series of eleven subjects who were examined in the sitting position by this method, average blood pressure in the brachial arteries 118 systolic, 76 diastolic in millimeters of mercury, intra-ocular pressure average 17

right and 17.5 left, showed retinal blood pressure in the central artery to average 68.2/32.2 mm. of mercury in the right eye, and 67.4/32.2 mm. of mercury in the left eye. These figures are lower than those obtained by other workers using the methods of Bailliart and Seidel.

8. In subjects examined to determine the influence of posture on retinal blood pressure a marked increase in retinal diastolic pressure was noted as the subject changed from the standing to the prone position.

9. Jugular compression caused a marked increase in cerebrospinal fluid pressure, which was accompanied by a marked rise in the diastolic pressure in the retinal arteries of four patients examined.

10. Repeated study of the blood pressure in the central retinal artery aids in the establishment of an early diagnosis of increased intracranial pressure in the absence of papilledema. When a diagnosis has been established, the method aids by making possible observations on augmentations and remissions of pressure.

11. In cases in which brain tumor is suspected, as spinal puncture is conceded to be dangerous, study of retinal blood pressure may aid in determining the presence or absence of increased intracranial pressure and for noting changes in pressure in the absence of papilledema.

30 East 40th Street.

CHANGES IN THE BRAIN IN INCREASED INTRACRANIAL PRESSURE *

GEORGE B. HASSIN, M.D.
Professor of Neurology, University of Illinois College of Medicine; Histologist to Illinois State Psychopathic Institute; Attending Neurologist, Cook County Hospital
CHICAGO

Increased intracranial pressure may be produced experimentally or by pathologic conditions, such as abscesses or tumors within the skull cavity. The latter were utilized by me in the present studies. Of seventeen tumors studied, four were meningeal and pressed on the hemispheres in the frontal, occipital, temporal and parietal regions; four were infiltrating (one of the frontal lobe and three of the basal ganglia); three were of the pons (one of these involved the fourth ventricle); two were in the cerebellopontile angle; three were multiple (hypernephromas), and one was a tuberculoma. In addition, material from a number of carcinomatous metastatic tumors of the brain, previously studied and reported,[1] has been used.

The majority of the tumors affected the brain by pressing on it from the outside, that is, they were extracerebral. Occupying space normally filled by brain tissues, they caused increased intracranial pressure and created conditions similar to those produced experimentally by the injection of fluids between the skull and the dura, by the filling up of this space with warm wax or with bags filled with mercury and by similar procedures. The extracerebral tumors, for that reason, were more suitable than the intracerebral, infiltrating types, such as gliomas, tuberculomas or metastatic carcinomas. As pointed out elsewhere,[1] the changes caused by the latter variety are either mechanical, the result of direct pressure by the tumor mass, or biochemical, which for want of a better term were designated toxic encephalitis. Such tumors were utilized for control or contrast studies, the main interest having centered into tumors of the former variety in which the outstanding clinical phenomena were those of increased intracranial pressure.

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* From the Pathology Laboratories of the Research and Educational Hospitals, University of Illinois, and the Illinois State Psychopathic Institute.

* Read at the Seventh Annual Meeting of the Association for Research in Nervous and Mental Disease, New York, Dec. 29, 1927.

1. Hassin, G. B., and Singer, H. D.: Histopathology of Cerebral Carcinoma, Arch. Neurol. & Psychiat. **8**:155 (Aug.) 1922.

Two examples of the pathologic specimens studied are shown in figures 1 and 2. Figure 1 represents an extreme grade of cerebral compression that resulted in severe pressure symptoms; figure 2 represents a more moderate and probably a more common degree. It seems proper to give a detailed outline of the changes that took place in the brain in each type; then, by contrasting them with the observations in the rest of the

Fig. 1.—Invasion of the frontal lobe by a pial endothelioma. This lies in a niche formed by destroyed and atrophied brain tissue.

series one may be able to arrive at some conclusions as to the histologic changes that are caused by increased intracranial pressure.

In both instances, the tumors produced depressions in the brain substance. In case 1, the depression was large and occupied almost one third of the basal portion of the frontal lobe (fig. 1). It almost encircled the tumor, but was not adherent to it. It was irregular in shape and its walls

were composed mainly of the white substance of the brain. In other words, the walls of the niche were remnants of that part of the brain which bore the brunt of the pressure and which had been replaced by the tumor. The tumor exercised on the brain a direct, purely mechanical pressure which was greatest, therefore, at this point. One may assume that the pressure decreased progressively as the distance from the tumor increased. For instance it must have been less in the parts of the brain between the walls of the depression and the skull, and still less in the neighboring portions, such as the parietal and temporal lobes. It must have been especially low in remote areas, such as the cerebellum, medulla, occipital lobe, caudal portion of the corpus callosum and basal ganglia.

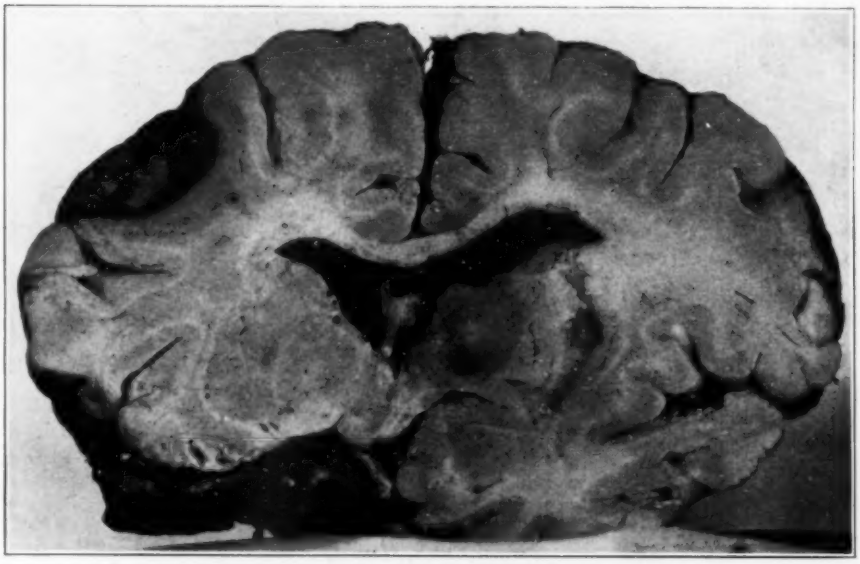

Fig. 2.—Depression in the cerebral cortex from pressure by a psammoma.

These areas were exposed not to a local, but to a remote intracranial pressure. The changes that resulted from both local and remote pressures were studied in celloidin, paraffin and frozen sections, with various staining methods. Of these, the methods of Holzer, Bielschowsky and Alzheimer-Mann proved especially valuable. The staining methods of Cajal and Hortega were unsatisfactory, probably because the material was old.

REPORT OF CASES

CASE 1.—*Pial endothelioma of the base of the frontal lobe.*

The walls of the cavity or niche that harbored the tumor were formed by a multitude of so-called cytoplasmic glia cells (fig. 3), homogeneous cell bodies, irregular in shape, possessing numerous processes and containing an eccentric nucleus rich in chromatin. The cell bodies were always of large size. Some

appeared as monster cells (fig. 4), with processes of great length and thickness (fig. 5), often arranged in thick bundles. A few cells, of smaller size, were somewhat vacuolated and resembled gitter-like structures. Many monster cells contained more than one nucleus which was sometimes unusually large and was often situated at the very edge of the cell body, while the processes were sometimes so abundant and massive that they appeared as a dense network covering the field.

Aside from the cytoplasmic glia, the walls of the niche contained numerous so-called glia nuclei (oligodendroglia cells) scattered over dense bundles of thin glia fibers mixed with blood vessels and capillaries. The oligodendroglia nuclei

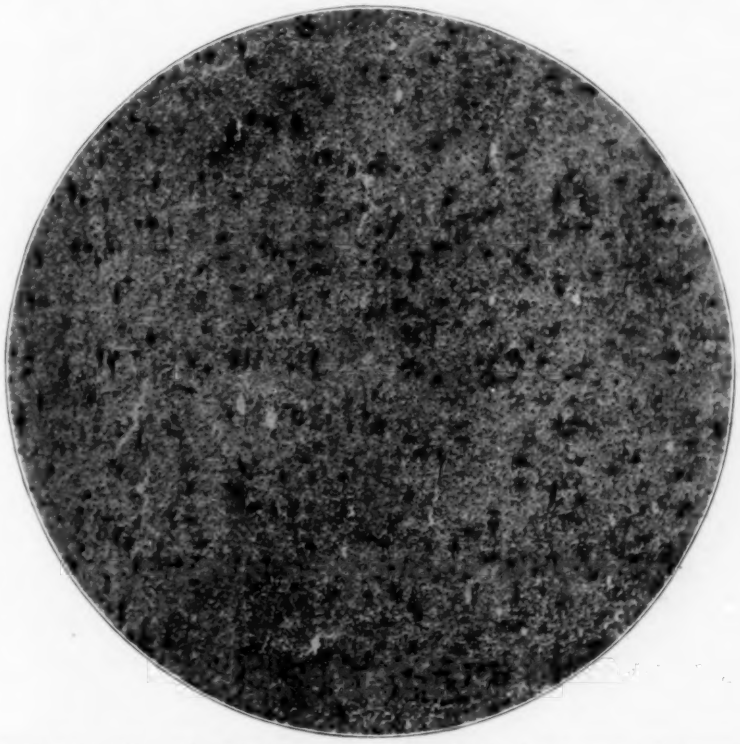

Fig. 3 (case 1).—The walls of the cavity enclosing the tumor. The numerous dark scattered formations are cytoplasmic glia cells; they are described in the text and reproduced under a higher magnification in figures 4 and 5. Holzer stain; × 50.

were large and rich in chromatin. Therefore, they appeared unusually bright and showed a distinct membrane. In some nuclei, the chromatin granules were rather scarce, but regressive changes, such as swollen oligodendroglia, were absent. Ganglion cells in these areas were scarce and were present only in some portions of the wall of the niche. They were in a state of necrobiosis and some effort was required to identify them. They appeared pale and vacuolated, and their processes were either swollen and homogeneous or broken up and missing.

Nerve fibers were absent; the blood vessels were hyperemic and congested, and their walls hypertrophied. Occluded blood vessels were not present, nor were

there signs of inflammation, such as plasma cells, lymphocytes and similar hematogenous elements. There were no foci of softening such as are seen in encephalomalacia, but many gitter cells filled with lipoids were present within the adventitial spaces of the blood vessels and in large numbers among the fibers or interspaces of the white substance. These were crowded with large globules and drops of lipoids forming masses that much resembled Jakob's β-type of gitter cells. The lipoid masses were so dense that the cell nuclei were overshadowed and could be seen only in exceptional instances. In short, the wall of the niche exhibited advanced degenerative phenomena and much resembled what is known as a glia scar.

Fig. 4.—Monster glia—a higher magnification of some glia cells reproduced in figure 3. Holzer stain; × 560.

Areas adjacent to the walls of the niche and situated between them and the cortex were fairly well preserved, with both the gray and the white substance well represented and defined. The ganglion cells exhibited the usual layers, but the subcortex showed a mass of cytoplasmic glia cells, blood vessels and well preserved nerve fibers. In some places, portions of gray matter were separated from the cortex by thick bands (fig. 6) of glia scar tissue. In general, the changes in the areas adjacent to the tumor were similar to those in the walls of the niche, but were rather less extreme. They also differed in containing so-called areas of rarefaction (fig. 7). These were of varying size, often situated around blood vessels and capillaries, and consisted of reticular tissue containing large vacuoles separated by delicate glia walls. They were usually empty but sometimes contained an amorphous, ill defined substance.

In the neighboring areas, the corpus callosum exhibited a number of degenerative phenomena varying from the formation of vacuoles to that of a glia scar. The vacuoles were, for the most part, empty, but many contained various types of gitter cells or other gliogenous formations, such as myeloclasts and myelophages. In addition, there were numerous cytoplasmic glia cells, oligodendroglia cells and accumulations of lipoids. The nerve fibers of the corpus callosum exhibited marked phenomena of secondary degeneration. The majority were merely

Fig. 5.—A monster glia cell with a thick, massive, branching process. Holzer stain; × 560.

tumefied, but in others the myelin was broken up into globules and enveloped by glia. Blood vessels and capillaries were numerous; their intima was hypertrophied, and the adventitial spaces were filled with lipoids. The changes described were present only in the cephalic portion of the corpus callosum (its genu), which was adjacent to the tumor. They may, therefore, be looked on as the result not of diffuse, increased intracranial pressure, but of the more direct pressure of the tumor itself. In the caudal portion (splenium) the changes were, in contrast, rather mild. They showed mainly in swollen oligodendroglia, vacuole formation, excessive vascularization and accumulation of lipoid substances. Oligodendroglia

cells were numerous. They were often arranged in long rows parallel to the blood vessels, and in many instances they appeared as if in pure culture. The spaces usually contained swollen oligodendroglia cells, many of which dropped out, leaving vacuoles (fig. 8), while many contained a generous amount of cytoplasm which was mostly finely granular (fig. 9). The blood vessels were numerous and, as a rule, patent; a few capillaries appeared partially occluded, and were accompanied by signs of softening in the surrounding parenchyma, but with masses of gitter cells in the adventitial spaces.

A condition similar to that in the corpus callosum was also encountered in the optic nerves and the chiasm. These structures were missing from the specimen in

Fig. 6.—Bundles of glia fibers forming a broad band in the cortex outside the destroyed area. Holzer stain; × 120.

this case, but they were studied in other cases of increased intracranial pressure. In them, the changes were practically the same as those described in the walls of the niche (fig. 10), that is, there was advanced degeneration of the nerves and glia scar formation.

In the remote areas (occipital lobe, cerebellum and medulla oblongata), the changes were mostly in the subcortical white matter, in the form of excessive glia proliferation (fig. 11); the gray substance showed satellitosis and neuronophagia. In the occipital lobe, the subcortex was excessively vascularized, and, in addition, exhibited numerous areas of rarefaction, mostly around the blood vessels and capillaries. The areas of rarefaction were also in evidence in the basal ganglia which otherwise did not show any changes in particular. I wish also to call

attention to the condition of the cerebellar hemispheres. The left was macroscopically smaller than the right, probably because it was subject to higher pressure. Microscopically, it exhibited much more extensive changes than on the right side, and these were especially in evidence in the white substance (fig. 11).

The subarachnoid space, as a rule, was greatly distended; the pial blood vessels were hyperemic and often surrounded by extensive hemorrhages. It was rich in cell elements, such as lymphocytes, mesothelial cells, fibroblasts and gitter cells. The choroid plexus showed swollen tuft cells which were expanded and in many instances resembled gitter cells.

Fig. 7.—Areas of rarefaction (cortex). Van Gieson; × 70.

Of the cranial nerves only the fifth, sixth and seventh were studied. They did not show any changes.

Comment.—From this review of changes in the areas remote from the tumor one may gather that they resembled essentially those present in the areas which were exposed to the direct pressure of the tumor. In other words, the changes that were caused by the increased intracranial pressure were practically of the same kind as those produced by pressure of the tumor itself. The differences were quantitative rather than qualitative; in both conditions, the changes were degenerative, mechanical in origin and proportionate to the severity of the pressure. They were

marked near the tumor, but gradually subsided in the areas farther away from it, and in some regions, such as the basal ganglia, were hardly noticeable.

The changes here described, especially those near the tumor, in the frontal portion of the corpus callosum and in the optic nerves are irreparable. They should, however, be expected only in cases in which the intracranial pressure is high, or in which it has been of long duration. When these factors are not marked, the changes in the brain are much

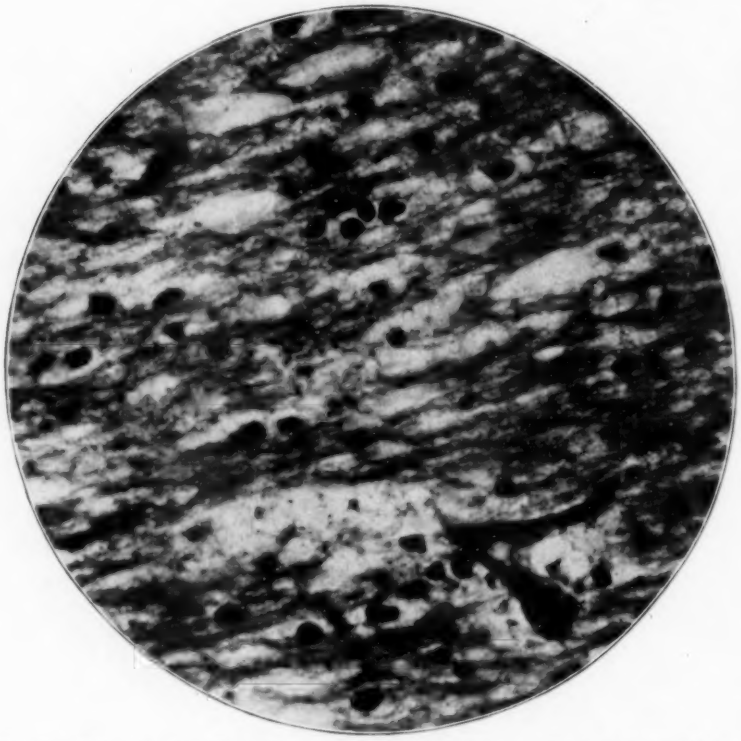

Fig. 8.—Oligodendroglia cells and vacuoles, some of which are devoid of contents, in the corpus collosum. Holzer stain; × 560.

milder and may recede to end in recovery. Such changes were present in the following case.

CASE 2.—*Calcified endothelioma (psammona) of the dura.*

In this case a depression (fig. 2) was produced in the left second frontal convolution by a calcified tumor of the dura (1 by 1¼ inches [2.5 by 3.1 cm.]). The niche produced by the tumor was not as deep as that in the previous case, and the surrounding tissues were not destroyed. Not only did the brain retain its normal shape, but even the sulci and the convolutions were normal. The left lateral ventricle appeared shorter than the right, which was somewhat elongated. This collapse of the left ventricle evidently was caused by the pressure and it made

room for the tumor. In case 1, room was made by atrophy of the compressed brain tissues.

On microscopic examination, the depressed cortex exhibited a normal array of layers. The subpial layer or stratum zonale appeared rather wide and contained numerous astrocytes. The ganglion cells exhibited mild degenerative phenomena, such as chromatolysis, homogeneous tortuous processes and neuronophagia. The majority contained numerous blue granules which covered the cytoplasm densely, invaded the dendrons and the glia and were also abundant in the walls of the blood vessels and capillaries (fig. 12). These were numerous and hyperemic without any signs of inflammation or other changes. Sections stained with the method

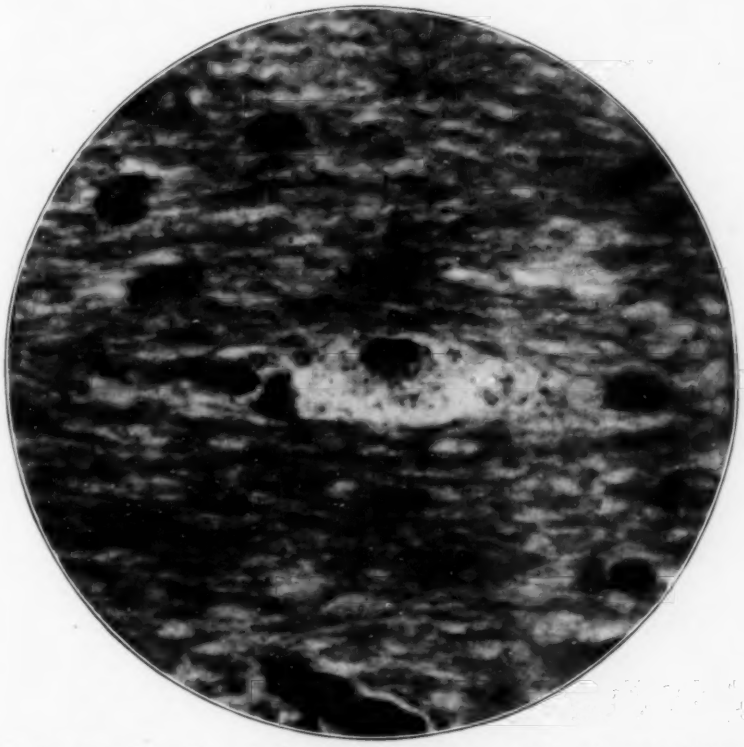

Fig. 9.—Granular glia cell within (in the center of the picture) a distended tissue space from the corpus callosum. Holzer stain; × 1,000.

of Holzer[2] exhibited numerous vacuoles, a great number of spider cells in the subcortex, an enormous increase in glia nuclei (oligodendroglia) and excessive cortical and subcortical vascularization. The pial vessels were also markedly hyperemic; the lumens were patent and the walls hyperplastic. The pia-arachnoid was distended, and its meshes enclosed large hemorrhagic foci around distended blood vessels.

In the large ganglia, the right caudate nucleus (on the side opposite the tumor) contained a fairly large focus of softening and numerous areolar foci. These foci of rarefaction were in evidence also in the left caudate nucleus, as well as in the optic

2. Holzer's method was used in the modification of Warkany, J.: Zur Methodik der Gliafärbung, Ztschr. f. wissensch. Mikr. **41**:508, 1924.

thalami and the corpus callosum. The latter also contained many vacuoles, mostly without contents, and masses of glia cells arranged in foci. Many of the glia cells had an expanded cytoplasm, faintly stained and homogeneous, without processes and with a peripheral nucleus rich in chromatin. Such expanded cells, mostly adendritic, are what the German authors designate as "gemästete" cells. Other cells were revealed as swollen oligodendroglia (fig. 13). The oligodendroglia cells were often so dense that they resembled Nissl's "Gliarasen"—several cytoplasmic glia cells are blended and appear as one protoplasmic cell body with several nuclei. They were also numerous in the medulla and were usually loaded with blue pigment granules. In the subependymal regions the foci were prominent and the glia

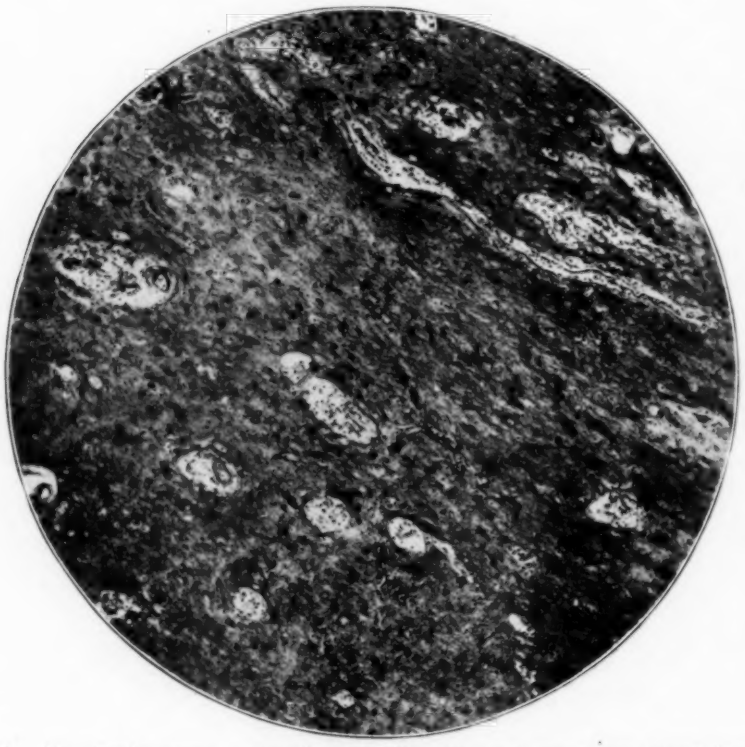

Fig. 10.—Optic nerve. Cytoplasmic glia cells and numerous blood vessels; adventitial spaces are filled with lipoids. Scarlet red and hematoxylin; × 60.

was mostly cytoplasmic. When stained with the method of Holzer, such cytoplasmic cells also appeared in the optic nerves, which were otherwise practically normal. No particular changes were found in other regions of the brain.

Comment.—The noteworthy changes in this case were softening of the left caudate nucleus, cytoplasmic glia in the subcortex, manifest glia reaction in the corpus callosum and marked areolar foci. Of these changes, the softening was the most serious, and it is rather remarkable that this focus was located on the side opposite to the tumor, where the intracerebral pressure must have been lower. In only one other case

(i.e., in two of the seventeen studied) did I find a focus of softening (in Ammon's horn). It is not, therefore, proper to consider this condition as a result of increased intracranial pressure, for it was absent in cases in which the pressure was extremely high. The increased pressure probably was, however, responsible for the other changes, such as the areolar foci and the glia manifestations in the corpus callosum and the subcortex.

Studies of the other cases showed that the pathologic changes vary in extent, as well as in intensity; that is, they may not be so far

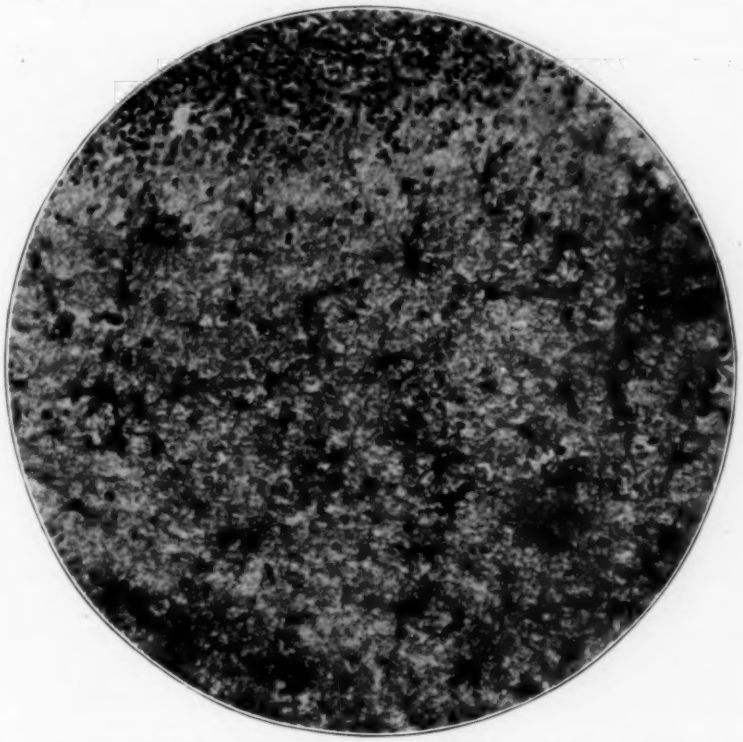

Fig. 11.—Cerebellum. Glia proliferation in the white substance. Holzer stain; × 170.

advanced as in case 1 and may be much more so than in case 2. Much depends on the localization of the original pressure. For instance, in a case of tumor of the fourth ventricle with severe pressure on the pons and a resultant enormous dilatation of the third ventricle and sylvian aqueduct, the ependymal cells were flattened, and the subependymal glia appeared fibrous, proliferated and dense. The blood vessels were hyperemic and distended, the walls were hypertrophied and the pons showed numerous areas of rarefaction. The corpus callosum, the optic

nerves and the subarachnoid space exhibited changes similar to those described in case 1.

In the case of a large tumor of the left temporal lobe (the clinical diagnosis had been dementia praecox), in addition to the observations described in case 1, basophil-metachromatic substances were present in the corpus callosum (fig. 14) with dense foci of oligodendroglia cells and an enormous vascularization of the compressed area. The degenerative changes in the corpus callosum, though present, were mild.

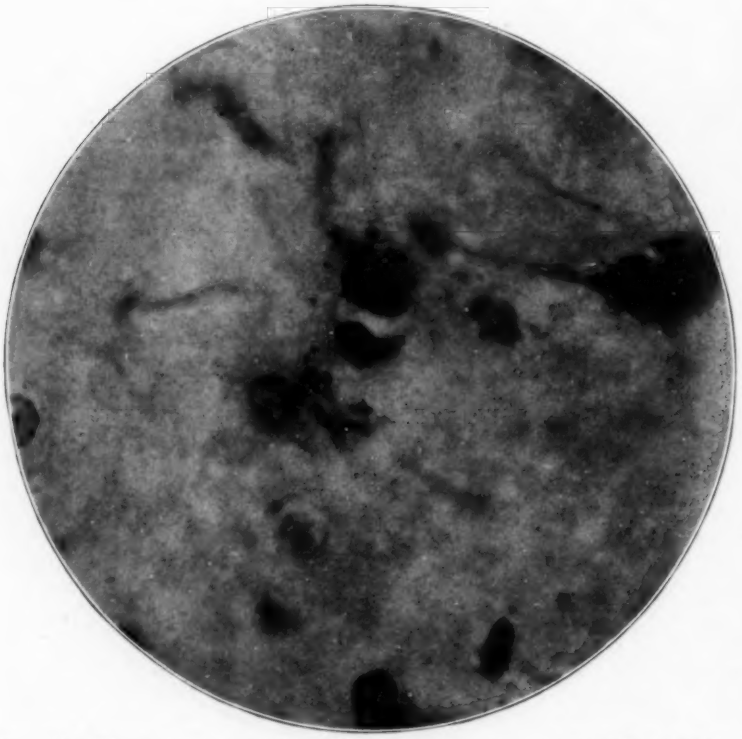

Fig. 12.—Blue granules within the ganglion cells, as described in the text. Toluidin blue; × 1,000.

Similar observations, including basophil-metachromatic substances, were also made in a case of tumor of the left cerebellopontile angle which formed a large niche and disfigured the cerebellum, the left temporal lobe and the medulla. Blood vessels here were numerous, often new formed, and the glia nuclei (oligodendroglia) showed features identical with those described in the corpus callosum.

In a case of infiltrating glioma of the optic thalamus, among other pathologic observations there were numerous small blue droplets and granules similar to those described in case 2. These were catabolic, or

"Abbau," products, probably what Alzheimer described as methyl blue granules. These, of course, were not mechanical but biochemical phenomena.

In general, changes produced by increased intracranial pressure from infiltrating tumors are somewhat similar to those described with extracerebral tumors, but they are much milder. The quantitative difference may be due to the fact that infiltrating tumors usually do not produce such displacement of the cerebral tissues with such great increase in the intracranial pressure as do the extracerebral tumors. Fundamentally, however, the changes are alike, though they vary in individual cases.

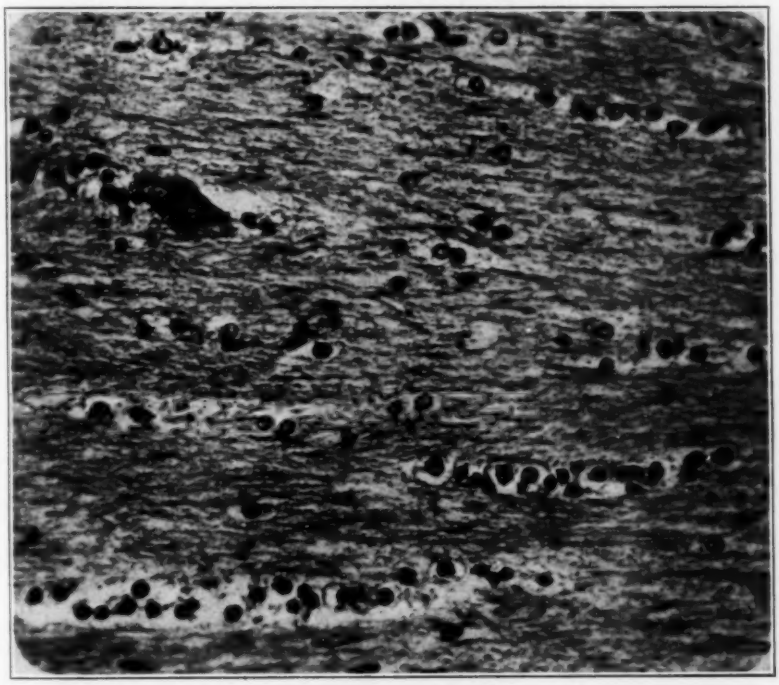

Fig. 13.—Swollen oligodendroglia arranged in rows. Holzer stain; × 350.

COMMENT

The changes observed in cases of increased intracranial pressure are: various stages of degenerative phenomena, with formation of glia scars and areolar foci or areas of rarefaction, irregularly scattered through the brain, including the corpus callosum; excessive vascularization with reactive proliferative phenomena in the vessel walls; degenerative optic nerve changes varying in extent and intensity; swollen oligodendroglia, and distended pia-arachnoid spaces which often contain a variety of cell elements.

It would not be amiss to present here a brief outline of changes in the spinal cord caused by increased intraspinal pressure. As figure 15 shows, the configuration of the spinal cord is preserved; the parenchyma is either broken up or occupied by vacuoles and areas of rarefaction or liquefaction; the gray matter is vascularized; the subarachnoid space is patent, and the pia, like the glia tissue, is hyperplastic. Other changes in the cord result from inflammatory conditions (perineuritis) of the meninges.

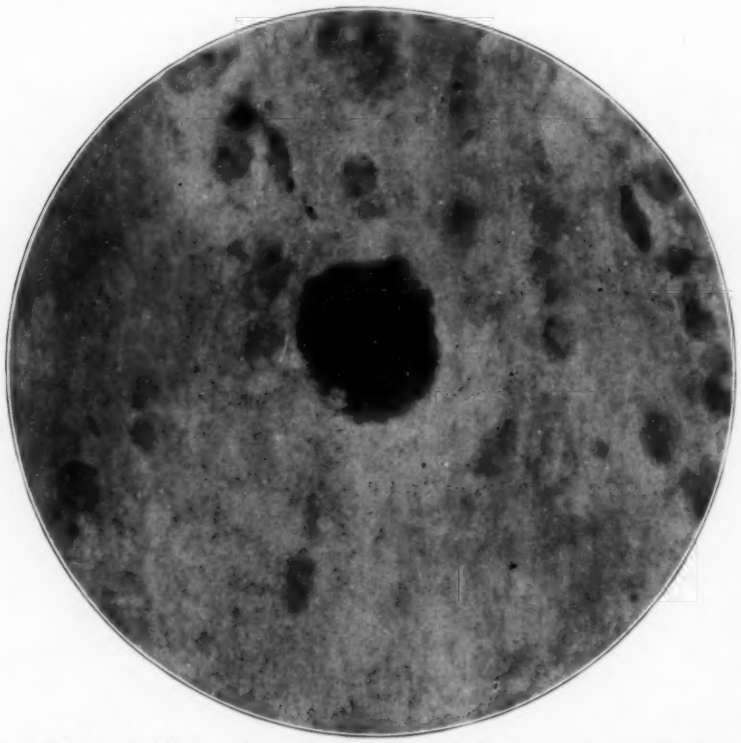

Fig. 14.—Basophil-metachromatic substances in the corpus callosum. Alzheimer-Mann stain; × 1,000.

The similarity between the changes caused by intracranial and intraspinal pressure is, thus, great; in fact, the changes in the two pathologic conditions are alike. The only difference is that the zones of rarefaction caused by increased pressure in the cord are more circumscribed than those in the brain where they are widely scattered. It is commonly agreed that the zones of rarefaction in the spinal cord are, as shown elsewhere,[3] the result of stasis of the tissue fluids from defective drainage.

3. Hassin, G. B.: Circumscribed Suppurative (Nontuberculous) Peripachymeningitis: Histopathologic Study of a Case, Arch. Neurol. & Psychiat. **20**:110 (July) 1928.

It is highly probable that in the brain the rarefied areas—the vacuoles and zones of rarefaction—are of analogous significance; that is, they are the result of defective drainage of some portions of the cerebral parenchyma. Large areas of the latter, however, not exposed to direct pressure, may be drained normally or with little interference by the tumor, or they may even be drained excessively. Such conditions may account for the fact that in the presence of even large tumors the clinical symptoms of increased intracranial pressure may be mild or absent altogether. On the other hand, local pressure on certain portions of the

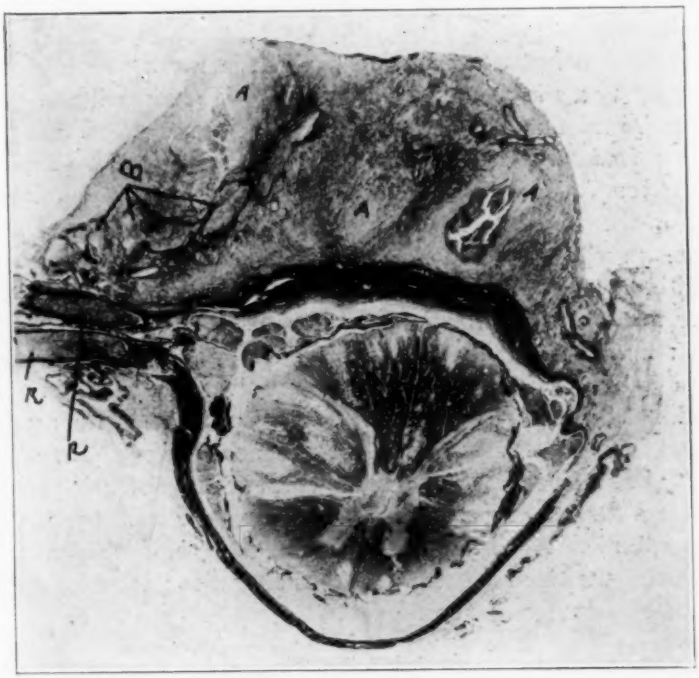

Fig. 15.—Spinal cord—pressure changes from an epidural mass containing three abscesses (*A*). The cord shows areas of rarefaction, a distended subarachnoid space and glia changes. *B*, encapsulated abscesses; *R*, the spinal roots. Van Gieson; × 5.

brain may affect the circulation of cerebral tissue fluids in areas remote from the tumor, cause their stagnation and thus be responsible for remote foci of rarefaction.

In general, the changes due to increased intracranial pressure may be classified as degenerative, associated with diffuse secondary proliferative glia phenomena. They are similar to the destruction of local nerve tissue caused by the prolonged mechanical pressure of a large tumor. In other words, their genesis is primarily mechanical. The changes in

the corpus callosum speak also in favor of the mechanical origin of the degenerations. In this area, the fibers appear to be damaged by the dilated lateral ventricles, torn by them—a condition not unlike the one produced in Anton's operation (sectioning of the corpus callosum). The more distended the ventricles the more numerous were the fibers that were degenerated, and vice versa. The fact that in some cases the genu of the corpus callosum was more damaged than the splenium may be explained on the assumption that here too the mechanical factors were more at play, for the lateral ventricles were more affected (dilated) in the cephalic than in the caudal portion.

When long standing and unusually severe, mechanical influences may lead to actual destruction and atrophy of the nerve tissues and their replacement by a glia tissue scar, as in case 1. In milder instances, as in case 2, no destruction obtains, but milder reactions occur. These are not unlike the changes found in contusion [4] and may also be classified as degenerative. In increased intracranial pressure, they are combined with changes in the tissue spaces, lateral ventricles and blood vessels. Such conditions may lead to what Adamkievicz [5] called condensation, so well revealed in figure 2. Here the bulk of the brain tissues becomes smaller in order to make room for the tumor mass.

The remarkable fact that the subarachnoid space remains patent and even is dilated can be explained by the reactive phenomena in the pia-arachnoid. Stimulated by the slow growth of the tumor, the connective tissue and other constituents of the subarachnoid space proliferate. The same may be said of the blood vessels which are consistently patent and hyperemic; often they are excessive in number, their walls hypertrophied and hyperplastic. Not in any instance did they show phenomena that would justify the claim that the histologic alterations noted were merely the result of vascular changes.

CONCLUSIONS

Increased intracranial pressure produces typical histologic changes in the brain.

The changes are degenerative, associated with reactive glia phenomena and are analogous to the changes that result from prolonged pressure (by a tumor) on the brain or spinal cord.

In the corpus callosum, optic nerve, chiasm and optic tract, the changes are diffuse and noticeable; in the ganglion cells, they are mild.

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4. Hassin, G. B.: Histopathologic Changes in Spinal Contusion, Arch. Neurol. & Psychiat. **13**:369 (March) 1925.

5. Adamkievicz, A.: Die Lehre vom Hirndruck und die Pathologie der Hirncompression, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturwissensch. Classe, Wien. **88**:11, 231, 1883; Ueber Gehirndruck und Gehirncompression, Wien. Klin. **10**:201, 1884.

The degenerative changes are combined with areas of rarefaction which are due to stasis of tissue fluids and accumulation, in some instances, of catabolic products, such as basophil-metachromatic substances, lipoids and methyl blue granules.

The extent of the changes varies according to the intensity and the duration of the increased pressure.

The histologic changes in pressure are of mechanical origin and are due, as in the corpus callosum, to the actual tearing of nerve fibers or to nutritional disturbances brought on in some parts of the brain by stasis of the tissue fluids.

The subarachnoid space and the blood vessels usually exhibit proliferative reactive phenomena.

When due to tumors, the changes produced by increased intracranial pressure are more marked in extracranial than in intracerebral types of tumor.

PROGRESSIVE DEGENERATIVE SUBCORTICAL ENCEPHALOPATHY

(SCHILDER'S DISEASE) *

JOSEPH H. GLOBUS, M.D.
AND
ISRAEL STRAUSS, M.D.
NEW YORK

In 1922, we presented before the American Neurological Association [1] the clinical and pathologic observations in a case which we termed progressive subcortical encephalopathy. Clinically, the case (that of a child) was characterized by an acute onset and progressive development of generalized spasticity and mental deterioration, followed by convulsive attacks and other features of a decerebrate rigidity as terminal events. The anatomic alterations were striking. They were degenerative and, although diffuse and widely distributed, were nevertheless distinctly limited to the white substance (subcortex) of the cerebral and cerebellar hemispheres. The gray matter was undisturbed and was without the slightest suggestion of disease.

Since that time, three more cases of similar character have come under observation. They are all so strikingly alike anatomically and have so much in common clinically that we are presenting them as members of a single group. In describing these cases, it is our aim to find and assign to them their proper nosologic position. This is particularly desirable since the reports of a fairly large number of cases which bear a very strong anatomic and clinical resemblance to those that are described here have recently appeared in the literature.

REPORT OF CASES

CASE 1.[2]—*History.*—V. A., a boy, aged 3½ years, had been small but healthy at birth; the parents and two other children were healthy. The patient had been well up to the age of 1 year, when he had a gastro-intestinal disturbance lasting three weeks, from which he made a good recovery. From then on, the child frequently cried out at night, but remained well otherwise until eight and a half

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* Read before the American Neurological Association, Atlantic City, June 3, 1926.

* From the Laboratories and the Neurological service of the Mount Sinai Hospital.

* Aided by a grant from the Emanuel Libman Fellowship Fund.

1. Globus, J. H., and Strauss, Israel: Chronic Progressive Subcortical Encephalopathy, Tr. Am. Neurol. A. **48**:351, 1922.

2. Dr. Oscar N. Schloss supplied the history and the pathologic material.

months before admission to the hospital, when he suddenly began to vomit. The vomiting, which lasted one day, was projectile in character, and there was a slight rise in temperature. This was followed by apparent recovery; the child took nourishment, was fairly well, and a week later was up and playing. At this time he fell from a chair and broke the left forearm. Good union of the fractured bone followed. Four weeks later the child fell from a chair again, and broke the other bone of the same arm. This also healed in good position. At that time it was noticed that the child's gait was becoming progressively impaired, and during the last three months he could hardly walk. His knees began to stiffen, and at night he cried and drew up his legs as if in pain. His condition gradually grew worse, and during the last months the arms also became spastic. He had spoken fairly well at the age of 2, but speech became gradually impaired and finally was completely lost. Four days before admission to the hospital, he developed a series of convulsive twitchings, lasting a few minutes at a time, involving first one part of the body and then another, and he screamed as if in pain. With this there developed a condition of apathy, disinterest in surroundings and finally semistupor.

Examination.—The child was fairly well developed; he appeared to be in a condition of stupor, from which he could not be aroused. The head was of average size. The ears were normal. The pupils were slightly dilated, but reacted to light. The left fundus showed engorgement of the vessels, and the disk was slightly blurred. The right fundus also showed engorgement of the vessels, but the disk was clear. There was slight ptosis of the left upper eyelid and flattening of the left side of the face. The chest was somewhat rachitic. There was evidence of beginning bronchopneumonia. The hands and arms were in a position of pronation and flexion; the legs were in spastic contracture, adducted and flexed (crossed). The child occasionally was thrown into a tonic convulsion which lasted a half minute at a time. This convulsion was easily brought on by any slight stimulation.

A definite diagnosis was not made during the life of the patient, though some form of diffuse cerebral lesion was suspected.

CASE 2.—*History.*—V. A., a boy, aged 1 year, was of normal birth and delivery and had been breast-fed up to the age of 5 months. The parents and one other child were well. At the age of 5 months the patient developed an acute disturbance of the gastro-intestinal tract, which was associated with difficulty in voiding urine. To relieve this condition, circumcision for phimosis was performed. Soon after this the child commenced to have frequent convulsive seizures. He was taken to a hospital, where an acute purulent otitis media was discovered, and the convulsive seizures were thought to be due to an inflammatory process in the brain. The ear was incised and drained, but this did not arrest the progress of the illness. The patient continued to lose ground, became exceedingly emaciated and developed opisthotonos and generalized rigidity with contractures.

Examination.—The infant, though 1 year old, looked more like a child of 6 months. He was markedly wasted, extremely fretful and cried continuously. The head was retracted so that the occiput touched the back. The pupils were dilated and reacted to light and in accommodation, but the child was blind. The extremities were rigid. The upper extremities were flexed at the elbows and held stiffly against the body. The hands were flexed at the wrists with the thumbs turned inside of the rigidly closed fists. The lower extremities were extended and rotated inward and crossed. There was marked hyperacusis.

Course.—The child displayed frequent convulsive attacks during which the generalized rigidity became more marked (fig. 1). Choreiform movements

appeared, which included facial grimaces, and were followed by clonic contractions of the extremities. During such attacks the child cried noisily, gasped and became profoundly cyanosed. These convulsive seizures, associated with the amaurosis, generalized rigidity, bilateral optic atrophy and pronounced wasting, suggested the diagnosis of diffuse subcortical encephalopathy. The cerebrospinal fluid was normal in all its phases including a negative Wassermann reaction. The patient continued to decline and died eight months after the onset of the illness.

Case 3.—*History.*—R. Z., a girl, aged 9 months, had been normally delivered. Her parents were well. The Wassermann reaction of the mother's blood was negative. There were no other children and no miscarriages. The patient's development was uneventful, except that the mother had noticed ever since birth that the child's head was somewhat larger than normal, and that, in spite of apparent health, the infant was not able to sit up or to support her head.

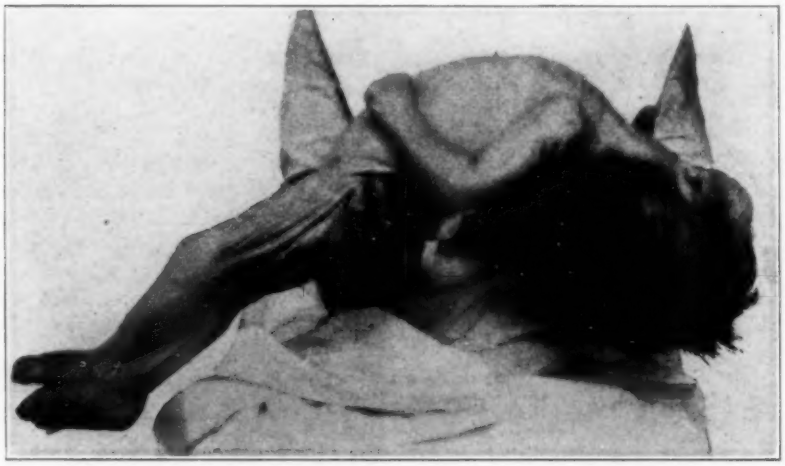

Fig. 1.—The infant in case 2 in a state of decerebrate rigidity.

Examination.—The infant was rather obese, lay quietly in bed, breathed normally and apparently was not acutely ill. Her head appeared considerably larger than normal. Its circumference was 49.5 cm. The posterior fontanel was closed, the anterior fontanel was open and felt somewhat full. The canal and drum of the left ear were normal. The canal of the right ear was filled with seropurulent discharge. The drum was flat and the landmarks were visible. The pupils were equal and regular; they reacted readily to light. The ocular fundi were normal. The abdominal reflexes were present and equal. The knee reflexes were hyperactive and equal. Repeated lumbar punctures revealed clear cerebrospinal fluid under moderately increased pressure, containing from six to eight cells per cubic millimeter. The Wassermann reactions of the blood and spinal fluid were negative.

Course.—The child's condition declined rapidly. Spasticity of the extremities developed, and respiration became noisy and labored, though the lungs did not reveal any abnormalities and the throat was free from exudate or redness. The right ear continued to discharge. This was soon followed by marked spasticity, rigidity of the neck, frothing at the mouth and convulsive seizures. A puncture

of the ventricle was then attempted through the fontanel, but fluid was not obtained. Further punctures were done to the left side of the first puncture. A needle was introduced anteriorly, straight inward and posteriorly up to the depth of 4 cm.; again cerebrospinal fluid was not obtained. It was concluded that there was no dilatation of the ventricular system, but it was decided that approach to the ventricles through the posterior horn was not justifiable in this instance. The child continued to grow worse. The extremities became spastic, and rather marked symptoms of the pyramidal tract appeared, with signs of meningeal irritation. The cerebrospinal fluid was still clear, with a slight tinge of yellow, but was under normal pressure and free from cells. The convulsions became almost continuous. The infant declined rapidly, and death occurred sixteen days after admission to the hospital. The diagnosis was internal hydrocephalus and purulent otitis media dextra.

Case 4.—*History.*—E. S., a girl, aged 6½ months, of normal birth and apparently normal development, breast-fed, a sister of another child who is well, had a slight rise in temperature two days before admission to the hospital. This was followed by repeated convulsions, generalized in character, which lasted for about twenty minutes at a time. The child soon began to vomit and displayed generalized rigidity. She was brought to the hospital where she was found to be acutely ill and apathetic. The deep reflexes were reduced. The cerebrospinal fluid was under normal pressure and gave a negative Wassermann reaction. The patient's condition continued to decline, and the diagnosis of encephalitis was considered. The patient died four days after the onset of the illness.

GROSS ANATOMY.

Case 1.—The cerebrum was firm and of a rubbery consistency, as though fixed in formaldehyde. There were no exudate, hyperemia, tubercles or thrombi in the meninges. Sections showed a yellow translucent appearance of the basal gangli. The white matter was much firmer than the gray. The cerebellum presented features similar to those of the cerebrum. The total weight of the brain was 1,120 Gm. The spinal cord was of increased consistency. The thymus, lungs, heart and spleen were normal. The liver had a mottled appearance caused by the presence of many pale gray, translucent areas. The kidneys were somewhat congested. The pancreas and gastro-intestinal tract were normal. The provisional anatomic diagnosis was diffuse gliosis of the brain.

Case 2.—The pia-arachnoid was smooth, glistening, moist and distended by a large amount of clear, colorless spinal fluid. The brain was rather small and heavy, weighing 510 Gm., and was of markedly increased consistency. The fissures were shallow and wide. The gyri were prominent.

Case 3.—The brain was markedly diminished in size, the gyri were prominent and the fissures were wide. The meninges were normal. The consistency was increased, giving the brain a leathery resistance on cutting. This was particularly true of the white matter.

Case 4.—The pia-arachnoid was somewhat edematous and injected. The subarachnoid space was filled with a clear, thin fluid. The convolutions of the brain were less prominent than normal. The brain felt somewhat soft and edematous. The ventricles were of normal size. There were neither areas of softening, nor areas of discoloration, but following fixation in formaldehyde, some alterations were noted in the white substance. The latter was granular and extremely brittle, having lost the smooth, uniform appearance of normal white matter.

MICROSCOPIC ANATOMY

CASE 1.—Though it would seem from the description of the gross anatomy of the cerebral hemispheres that both the cortex and the subcortex were equally involved in the disease process, it soon became apparent, on studying microscopic preparations, that the cortex was completely free from pathologic changes, while the subcortical layers, basal ganglia and the fibrous tracts in the brain stem were the seat of a most striking disease process. There was a clear line of demarcation between an apparently normal cortex and the diseased subcortical stratum, which was well demonstrated in preparations stained by the Marchi method

Fig. 2.—Section illustrating the distinct line of demarcation between the normal cortex (*C*) and the degenerating subcortex (*S*). Marchi stain; × 141.

(fig. 2). In such a preparation one could see diffuse massive accumulations of granules, stained black by the osmium, in the subcortical substance, which came to an abrupt termination where the subcortical layer abutted the cortex.

A higher magnification of a similar preparation showed that the dark, almost black, appearance of the subcortical layers was due to the presence of numerous diffusely scattered coarse black bodies (fig. 3), which on close scrutiny proved to be compound granular cells loaded with fat, stained by osmic acid. Preparations stained by the silver-carbonate method showed that many of the so-called compound granular cells were not as yet fully rounded up and did not present a uniform

granular appearance. They still contained numerous fine filaments and had a dense, circularly arranged layer of black granular deposit at the periphery, giving to the center a hyaline glossy appearance. They apparently were a transitional form of glia cells in their metamorphosis into compound granular (gitter) cells. Their character will be discussed together with other alterations in the glia.

In the brain stem, these accumulations of granular cells could be found only in tracts or fasciculi of fibers, and there, in accordance with the size of such fibrous

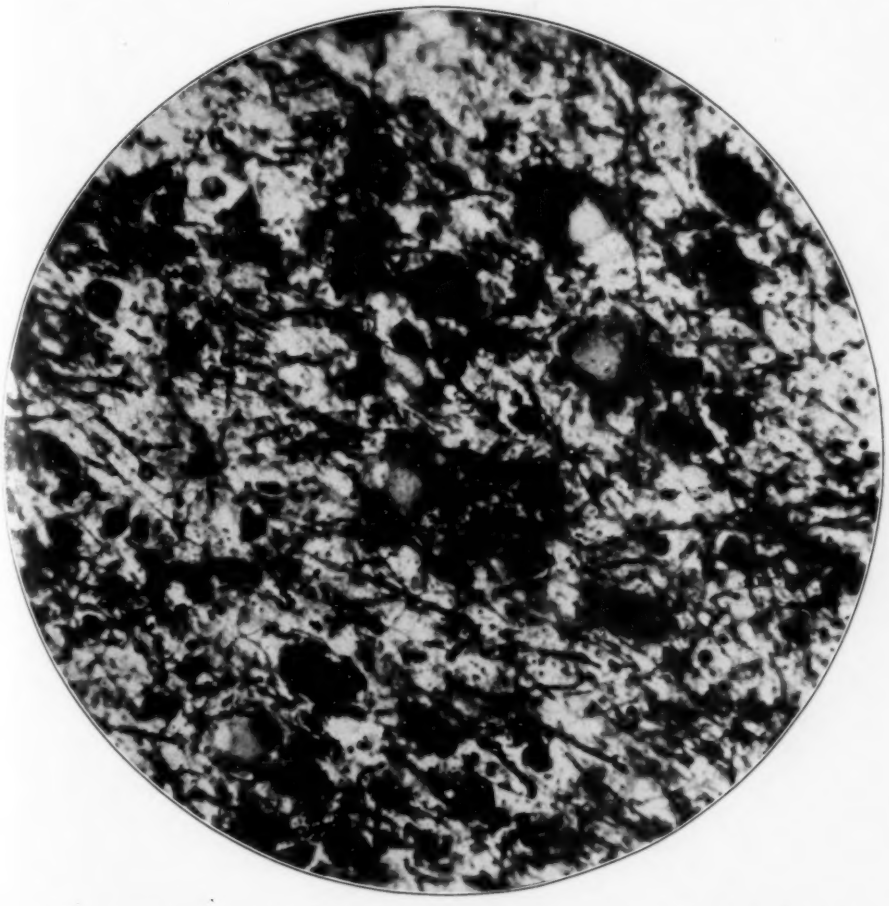

Fig. 3.—Section as in figure 1 under higher magnification, illustrating the character of the glial hyperplasia in the subcortex. It shows numerous compound granular cells, loaded with fat (stained black by the osmic acid). Marchi stain; × 500.

masses, they formed "islands" of degenerative processes which were variable in extent (figs. 4 and 5).

Throughout the white matter, there were striking alterations in the glial elements. These were widely distributed, showing slight local variation, which was most pronounced in the white substance directly beneath the cortical gray

matter and in cephalad portions of the brain stem such as the corpus callosum and basal ganglia. In the midbrain, pons and medulla oblongata the glial hyperplasia was not so marked and was limited to the fiber tracts.

The dominating type of glia was the large fiber-forming astrocyte (fig. 6 *A*). It was present in large numbers and active in the elaboration of glia fibers (fig. 6, *B* and *D*). Such astrocytes were found freely mixed with the almost equally abundant compound granular cells (fig. 6 *C*). Both types were also found,

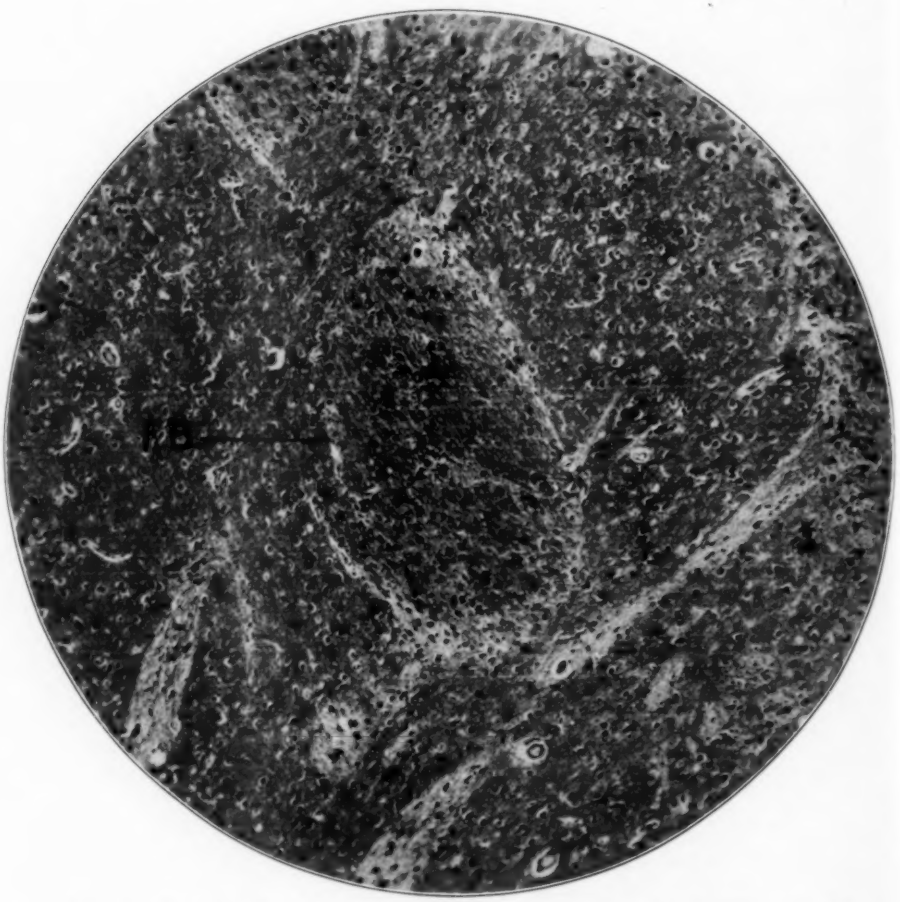

Fig. 4.—Section illustrating degenerative changes in isolated fibrous bundles *F. B.*; the black bodies are compound granular cells loaded with fat. Marchi stain; × 75.

as was already pointed out, in the neighborhood of fiber bundles throughout the entire length of the brain stem, including the medulla oblongata.

Throughout the white matter there were seen many small nuclei, some of which were surrounded by a fair amount of cytoplasm (fig. 6, *A* and *C*). They were largely microglia and oligodendroglia (fig. 7, *A* and *B*). Thus all forms of glia participate in the hyperplasia with the microglia actively engaged in the

formation of compound granular cells, a process which also has been observed in another degenerative disease of the central nervous system (Globus [3]).

The degenerative and the destructive process in the nerve fibers was so intense that it was practically impossible to determine whether we were dealing here with primarily a neurolytic process in the axis cylinders and a secondary myelin degeneration or with a primary myelin destruction and a secondary dissolution of the axis cylinder. Both conditions were found side by side. Thus, in all

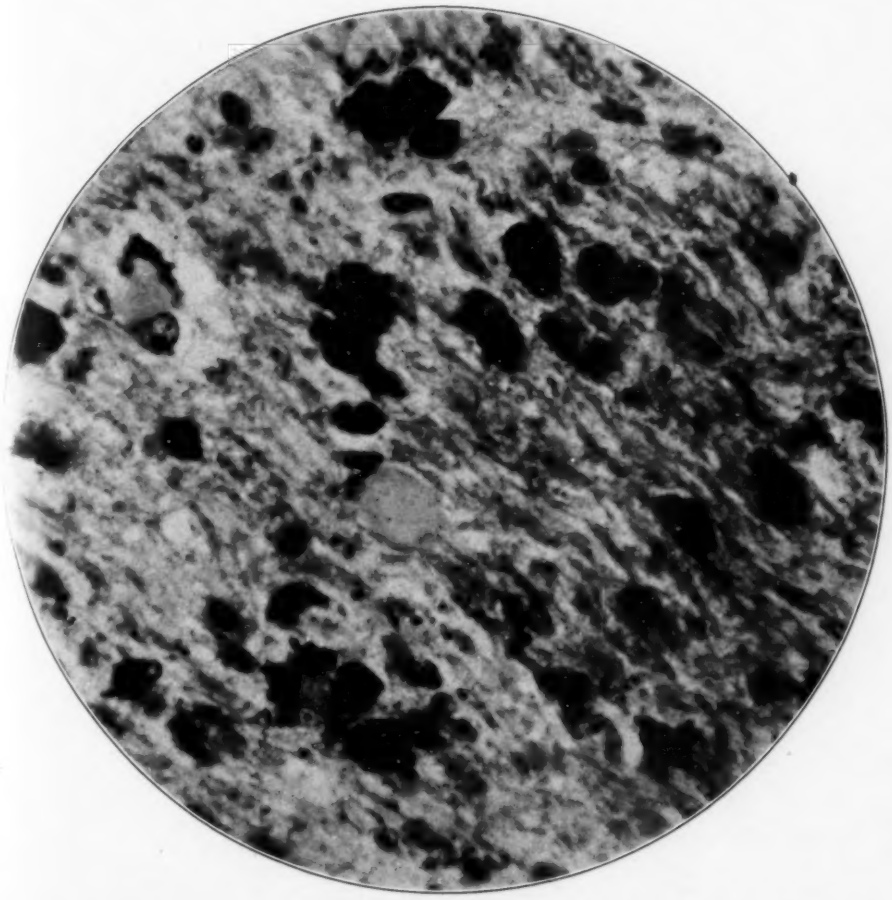

Fig. 5.—Section in figure 3 under higher magnification, showing the compound granular cells filled with fat (stained black by the osmic acid), and other glial elements. Marchi stain; × 725.

preparations in which osmic acid or the Spielmeyer myelin-sheath stain was employed, neurolytic phenomena were observed. Swelling of the axis cylinders (fig. 8), dumb-bell formations, ball-like terminations and corkscrew formations

3. Globus, J. H.: Glial Response in Chronic Progressive Degeneration of the Brain, Arch. Neurol & Psychiat., to be published.

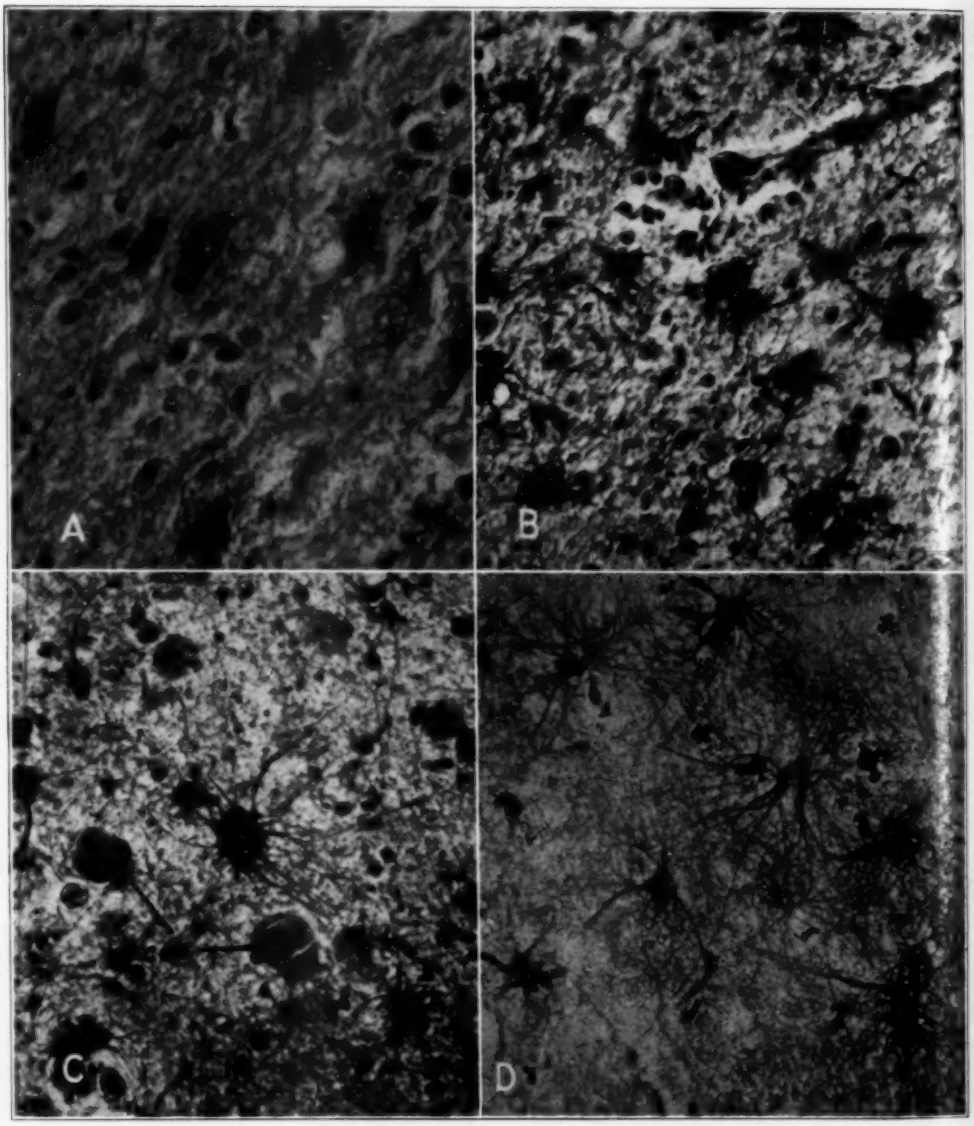

Fig. 6.—A series of photomicrographs showing in greater detail the glial activity in the diseased areas. *A*. Glial elements are brought out in this preparation by the iron hematoxylin stain. *B*. The same glial elements when stained by the Cajal gold-sublimate method (modified). *C*. Glial elements in the same zone brought out by the Hortega silver-carbonate method (modified). Here in addition to the astrocytes many compound granular cells (*C G C*) are seen. *D*. The fibroblastic character of many glial elements are well brought out here by the Weigert glia stain.

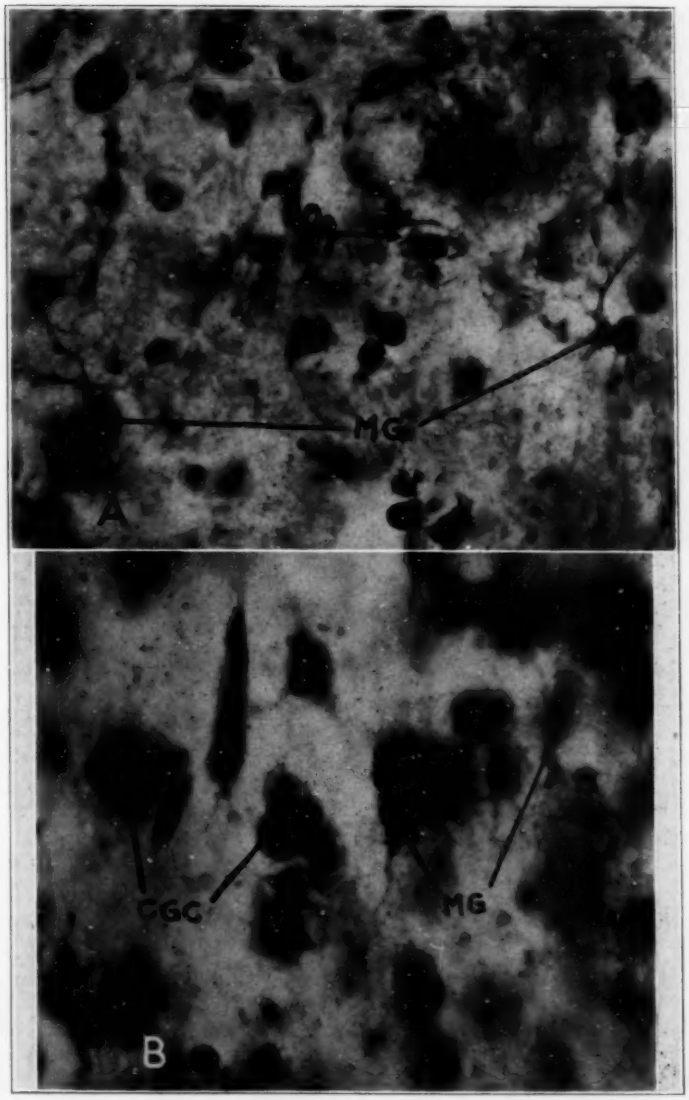

Fig. 7.—Microglial changes illustrated by preparations stained by the Hortega silver-carbonate method (modified); ×750. *A*. Showing a small group of microglia (*M G*). They are swollen and binucleated, with processes undergoing dissolution. *B*. Microglia (*M G*) in transformation into compound granular cells (*C G C*). Less numerous are the oligodendroglia (*O G*).

(fig. 9 *A*) were found everywhere in the field. These changes were not unlike those found by Martinesco and Minea,[4] and Hassin,[5] in disseminated sclerosis, and by Schimazono,[6] Wohlwill[7] and Globus and Strauss[8] in progressive funicular myelopathy (combined system disease). The swellings of the axis cylinders were occasionally surrounded by a fine ring of lipoid substance stained black with osmic acid. Numerous Elzholz bodies and compound granular cells, containing small quantities of finely granular material, in relatively large numbers, were found scattered among the degenerated fibers. Axis cylinders apparently devoid of myelin were frequently found. They were uniform in caliber, uninterrupted in their course, and free from any evidence of a degenerative process. Their presence was suggestive of a primary involvement of the myelin.

Throughout our material, the vessels showed uniform adventitial infiltration by compound granular cells (fig. 9 *B*). In the subependymal layer an occasional vessel was seen with its lumen almost completely obliterated by an organized thrombus. Around a few such small vessels the surrounding tissues were softened and infiltrated with extravasated blood, but such results were so infrequent that they hardly contribute to the pathologic picture.

The pia-arachnoid membrane showed definite thickening, with a moderate number of fibroblasts and some small round cell infiltration. These changes, however, were not regarded by us as an inflammatory process in response to bacterial invasion but rather in the nature of a reaction to irritation caused by a noxious product thrown into the subarachnoid space by the adventitial draining system of the cerebral blood vessels during the course of a degenerative process.

The gray matter of both the cerebral and cerebellar hemispheres was free from any recognizable morphologic alterations. The cell arrangement as well as the individual cells, was intact, and there were unusual changes neither in the glia (fig. 10, *A* and *B*) nor in the blood vessels.

Case 2.—In this case also the histologic study showed the unusual limitation of the disease process to the white substance wherever found. In the Weigert-Pal preparations (fig. 11), the staining property of the white matter was markedly reduced indicating an extensive loss of myelin. As in case 1, the sharply defined limitation of the lesion was well brought out by the various fat stains and was illustrated by the Herxheimer scarlet R. method (fig. 12). There were moderate local variations in the intensity of the degenerative process. In both parieto-occipital regions, destructive changes of a more recent and more acute character were found. The intensity of the process was shown by the character and density of cellular infiltration (fig. 13). Compound granular cells and rod cells almost completely replaced the normal brain tissue, but here also in spite of the progressive character of the process, it did not extend beyond the white matter of

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4. Martinesco, G., and Minea, J.: Contribution à l'histopathologie de la sclérose en plaques, Rev. neurol. **18**:957, 1909.

5. Hassin, G. B.: Multiple Sclerosis, an Investigation by the Association for Research in Nervous and Mental Diseases, New York, Paul B. Hoeber, 1921, vol. 2.

6. Schimazono, T.: Ueber das Verhalten der zentralen und der peripheren Nervensubstanz bei verschiedenen Vergiftungen und Ernaehrungstoerungen, Arch. f. Psychiat. **53**:972, 1914.

7. Wohlwill, F.: Zum Kapitel der pathologisch-anatomischen Veraenderungen des Gehirns und Rueckenmarks bei perniciose Anaemie und verwandten Affectionen, Deutsche Ztschr. f. Nervenh. **68**:38, 1921.

8. Globus, J. H., and Strauss, I.: Progressive Funicular Myelopathy (Subacute Combined Degeneration), Arch. Neurol. & Psychiat. **8**:366 (Oct.) 1922.

the hemisphere. Under higher magnification (fig. 14), the character of the cellular infiltrates was clearly brought out. The latter, as already noted, consisted mainly of compound granular cells, and transitional forms of glia cells, including the so-called rod cells. The relationship of the latter to the microglia of Hortega was well brought out by the silver-carbonate stain, which showed them to be a modified form of Hortega cells (fig. 15). While such changes are

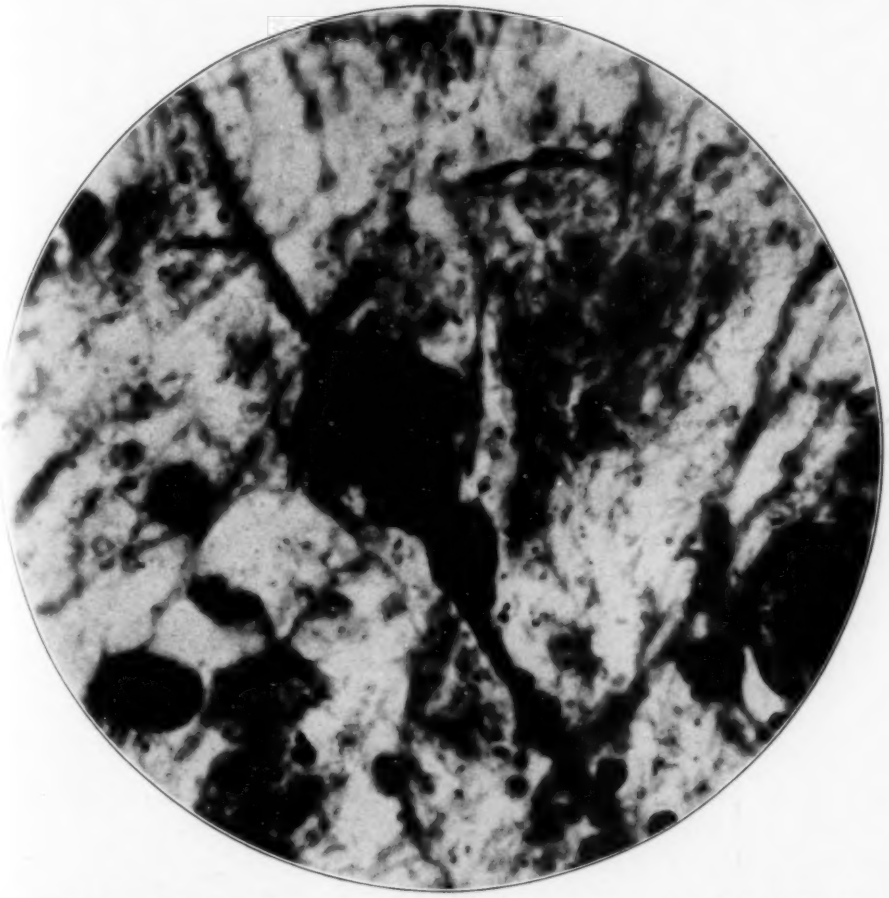

Fig. 8.—Bulbar swelling and granular degeneration of the axis cylinder. Marchi stain, counterstained by the Bielschowsky silver method; × 2,000.

most pronounced in the more acute lesions, the general character of the gliosis is that of a diffuse hyperplasia of fibroblastic astrocytes (fig. 16).

Case 3.—The histologic observations in this case were substantially the same as in cases 1 and 2 except for the fact that the gliosis was somewhat less intense (compare fig. 17 with fig. 16).

Case 4.—The pathologic changes in this case were, in the main, the same as in the previous three cases. They differed, however, in some details which were in

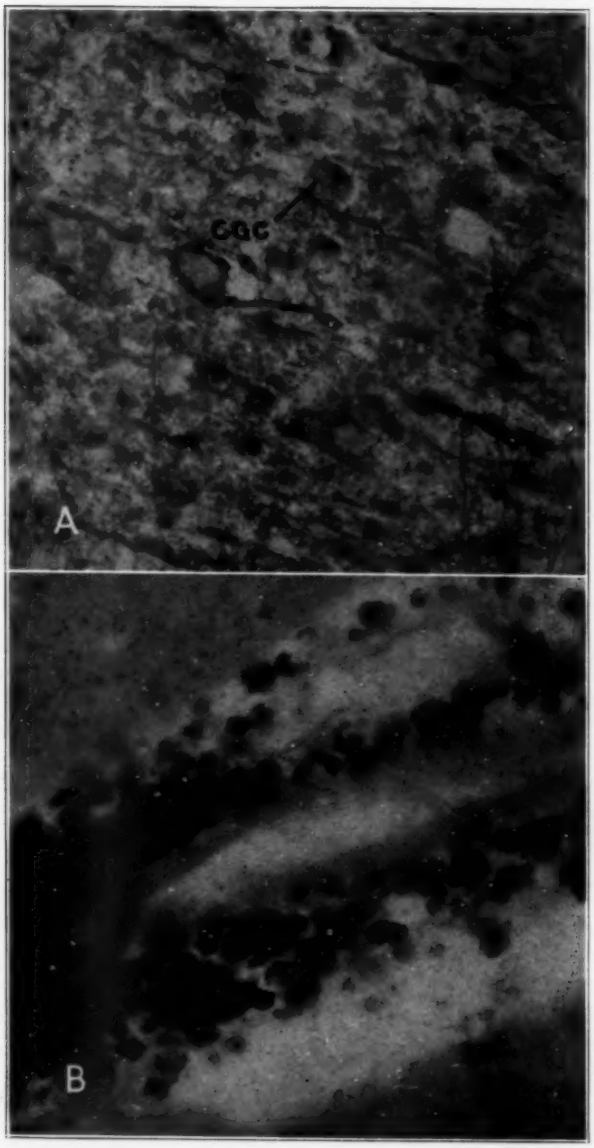

Fig. 9.—*A*. Swelling and distortion of the outline of the myelin sheath indicating degeneration of myelin. Compound granular cells *(C G C)* are seen in the vicinity of the degenerating myelin. Iron hematoxylin stain. *B*. A blood vessel with extensive adventitial infiltration. The cells are mainly compound granular cells filled with fat. Marchi stain.

accord with some of the gross anatomic variations. Here too, however, the disease process was limited to the white substance, but it was apparently of a more acute and destructive character. In Pal-Weigert preparations the destruction of the myelin appeared somewhat less uniform but was nevertheless diffuse throughout

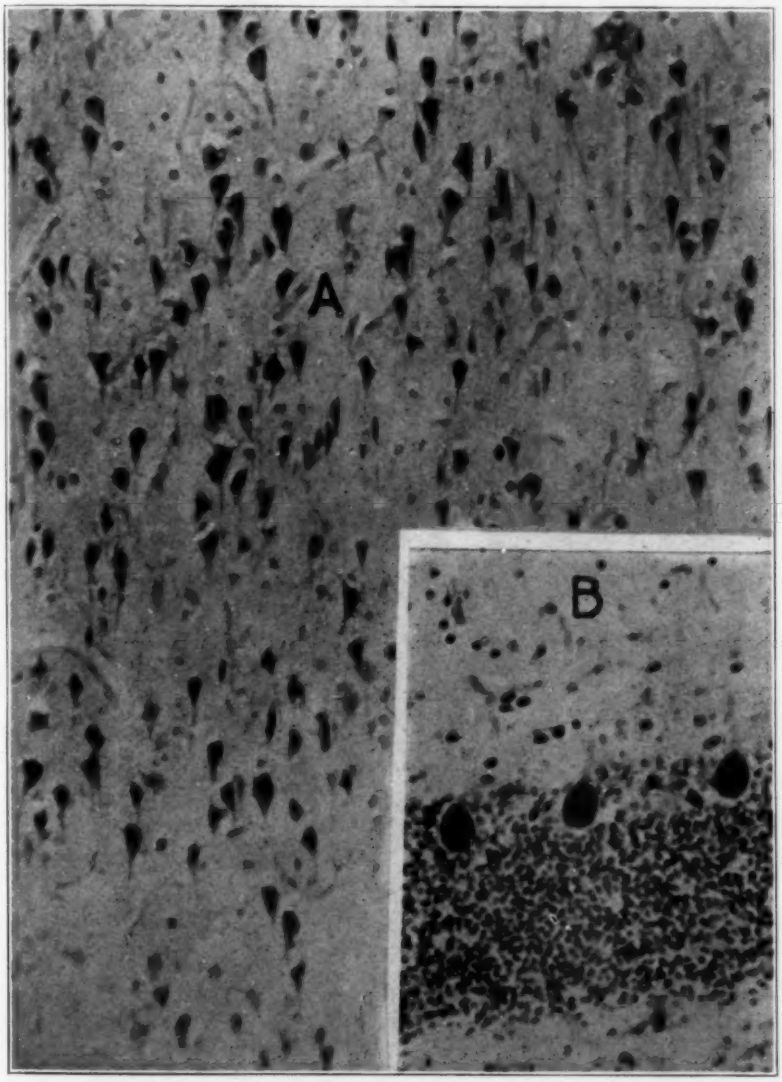

Fig. 10.—*A*. Normal cerebral cortex. Nissl stain; × 220. *B*. Normal cerebellar cortex. Nissl stain; × 330.

the brain (fig. 18 *A*). The loss or disruption of subcortical tissue was seen even under lower magnification and bore the character of the so-called "status spongiosus" (fig. 18 *B*). The glial alterations were also mainly of regressive character, with only mild progressive, diffuse hyperplasia and hypertrophy

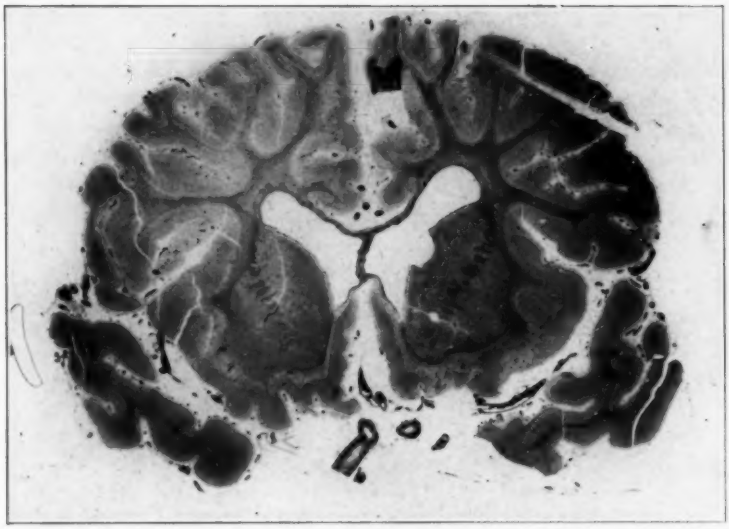

Fig. 11.—Coronal section of frontal lobes showing almost complete loss of myelin. Pal-Weigert stain.

Fig. 12.—Line of demarcation between normal cortex (*C*) and diseased subcortex (*S*). Herxheimer's scarlet R stain; × 40.

(fig. 19) in the involved areas. Mitotic division of glia with generalized glial hyperplasia was clearly seen in Nissl preparations (fig. 20, *A* to *D*). Transitional forms leading to the formation of compound granule cells were also found. The nerve cells were intact and well preserved in the cerebral cortex as well as in the stem ganglions and nuclei (fig. 21).

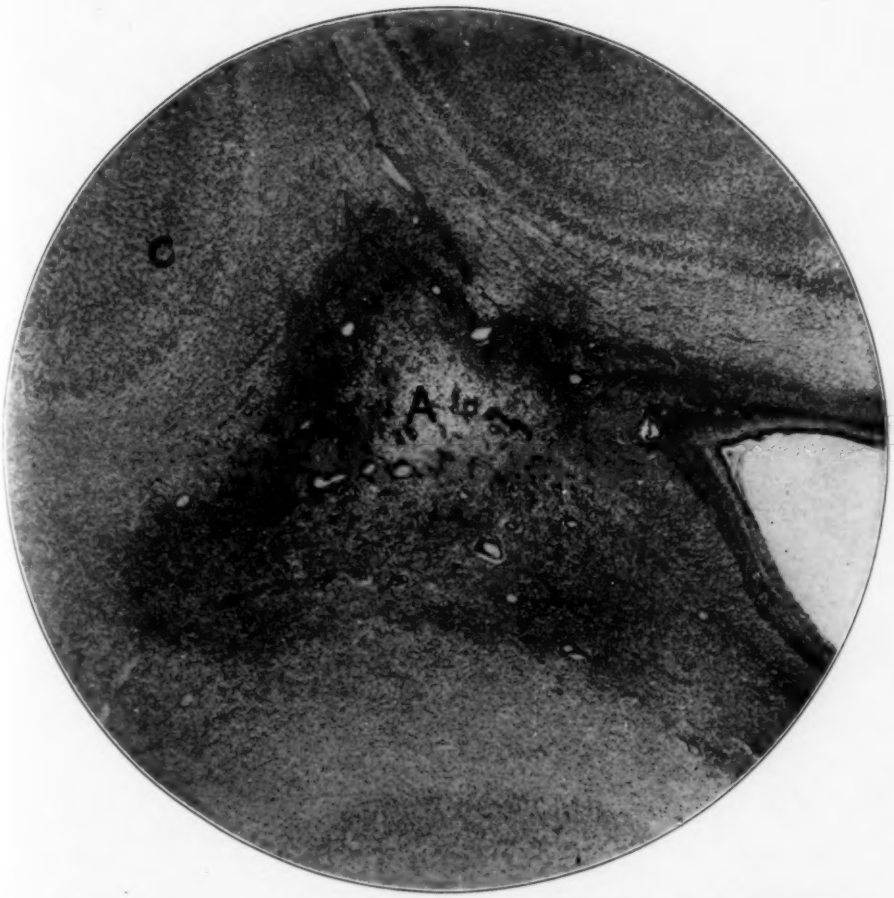

Fig. 13.—Subcortex in the region of the occipital lobes. The densely stained area (*A*) is the zone of the most pronounced disease changes. The cortex (*C*) is uninvolved. Nissl stain; × 17.

GENERAL ANATOMIC CONSIDERATIONS

The morphologic alterations might justifiably be grouped under the term of diffuse gliosis of the brain. This, however, is merely a name applied to cases in which diffuse hyperplasia is the end-result of several pathologic processes which may be inflammatory, degenerative or the result of defective development. Recently, attempts have been made

by more thorough histologic studies to evaluate the pathologic alterations in some of the members of this group so as to determine their true nosologic position. Thus, the so-called aplasia axialis extracorticalis diffusa of Merzbacher,[9] the interlobar symmetrical sclerosis of Marie and Foix,[10] the encephalitis periaxialis diffusa of Schilder,[11] the peri-

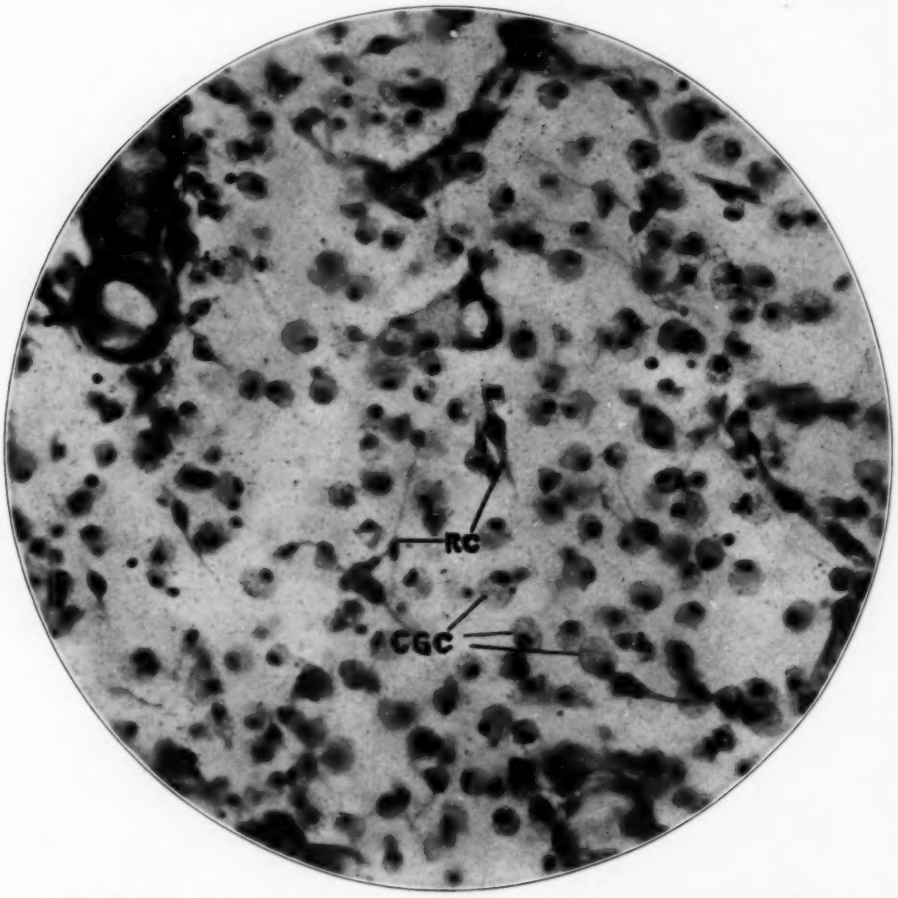

Fig. 14.—Section in figure 13 under higher magnification. Note the absence of inflammatory changes, such as perivascular small round cell infiltration, and the presence of many compound granular cells (*C G C*) and rod (*R C*) cells. The changes are mainly those of degeneration and softening. Nissl stain; × 300.

9. Merzbacher, L.: Eine eigenartige familiaer-hereditaere Erkrankungsform (aplasia axialis extracorticalis congenita), Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:1, 1910.

10. Marie, P., and Foix, C.: Sclérose intracérébrale centrolobaire et symmétrique, Rev. neurol. **27**:1, 1914.

11. Schilder, P.: Zur Kenntniss der sogenannten diffusen Sclerose (Ueber Encephalitis Periaxialis diffusa), Ztschr. f. d. ges. Neurol. u. Psychiat. **10**:1, 1912; Zur Frage der Encephalitis Periaxialis Diffusa (sogenannte diffuse Sklerose), ibid. **15**:359, 1913.

vascular myelin necrosis and the new form of infantile sclerosis of Krabbe,[12] the encephalomyelomalacia chronica diffusa of Hermel,[13] the encephaloleukopathia scleroticans progressiva of Flatau,[14] and the sclerosis and microcephaly of Freeman,[15] have become known. Under all these terms, with the possible exception of Freeman's material, a dis-

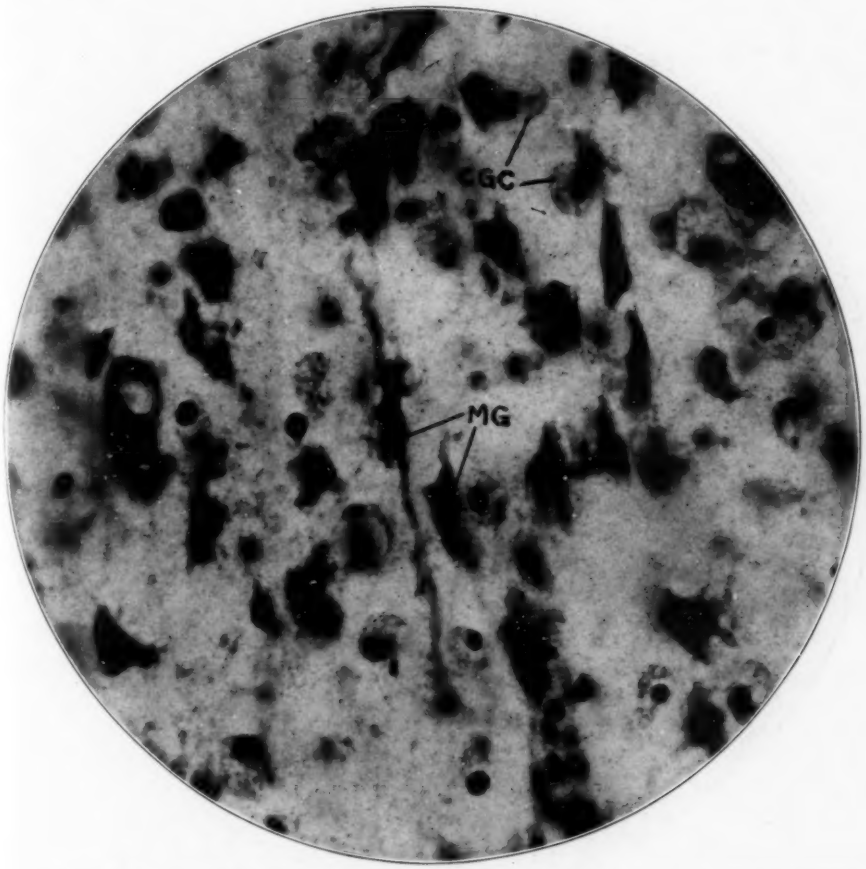

Fig. 15.—Formation of compound granular cells (*C G C*) and their derivation from microglia (*M G*) is illustrated here. Hortega silver-carbonate method (modified); × 600.

12. Krabbe, Knud: Beitrag zur Kenntniss der Fruehstadien der diffusen Hirnsklerose, Arch. f. d. ges. Neurol. u. Psychiat. **20**:108, 1913; A New Familial Infantile Form of Diffuse Brain Sclerosis, Brain **39**:74, 1916.

13. Hermel, H.: Ueber einen Fall von Encephalo-Myelomalacia chronica diffusa bei einem 4 jaehrigen Kinde, Deutsche. Ztschr. f. Nervenh. **68**:338, 1921.

14. Flatau, E.: Encéphalo-leucopathica scleroticans progressiva, Encéphale **20**:475, 1925.

15. Freeman, W.: Microcephaly and Diffuse Sclerosis, Brain **50**:189, 1927.

ease form was described in which widespread dissolution of myelin, with less complete destruction of the axis cylinders, and an extensive and uniform hyperplasia and hypertrophy of the glia was a striking feature. This, coupled with a lack of definite infiltrative or productive mesodermal reactions, presented, in our opinion, convincing proof of the

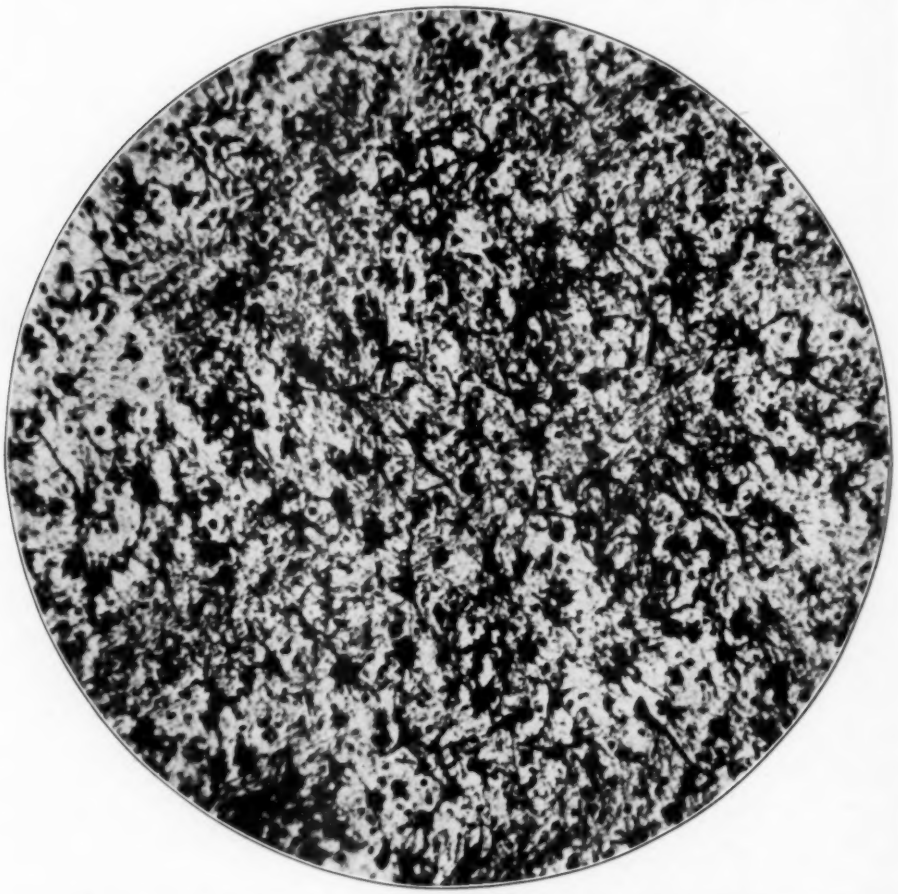

Fig. 16.—Intensive gliosis (glial sclerosis). Cajal's gold-sublimate stain (modified).

degenerative character of the process. But above all, the striking limitation of the pathologic process to the white substance of the cerebrospinal axis served to single out this disease from the large group of diffuse gliosis and made apparent the close relationship that exists between aplasia axialis extracorticalis, encephalitis periaxialis diffusa, perivascular myelin necrosis and the disease which we are describing under the name of progressive degenerative subcortical encephalopathy.

In the material of Merzbacher,[9] there was the same limitation of the pathologic changes to the white substance in the brain stem, but in the midst of the diffuse loss of fiber structure, islands or small aggregations of well preserved nerve fibers were found. These we have failed to observe in our case, though we have recorded the observation of a few

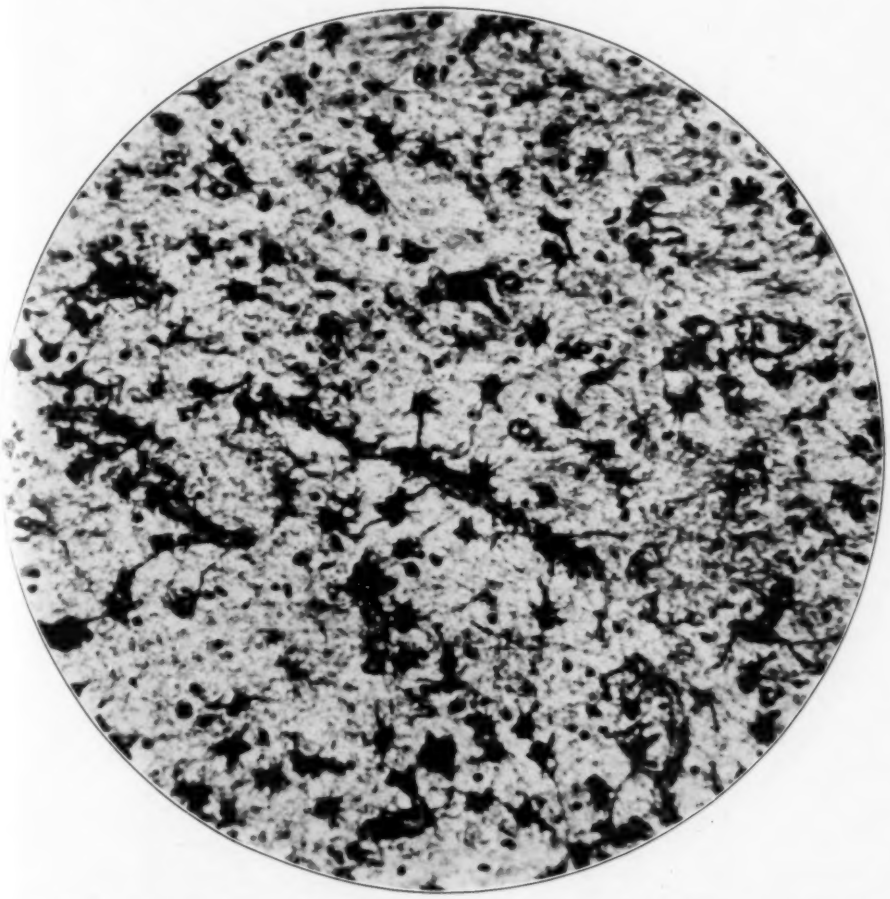

Fig. 17.—Glial sclerosis less intense. Compare with figure 16. Cajal's gold chloride sublimate method (modified); × 300.

groups of naked axis cylinders, which we regard as those which have temporarily escaped complete destruction.

Merzbacher also emphasized the lack of active glial proliferation in frankly diseased areas outside of the thalamus opticus. In the latter structure he found a fairly marked glial reaction. On these two facts, the presence of islands of relatively well preserved nerve fibers and the absence of a uniform glial reaction, he constructed his hypothesis that

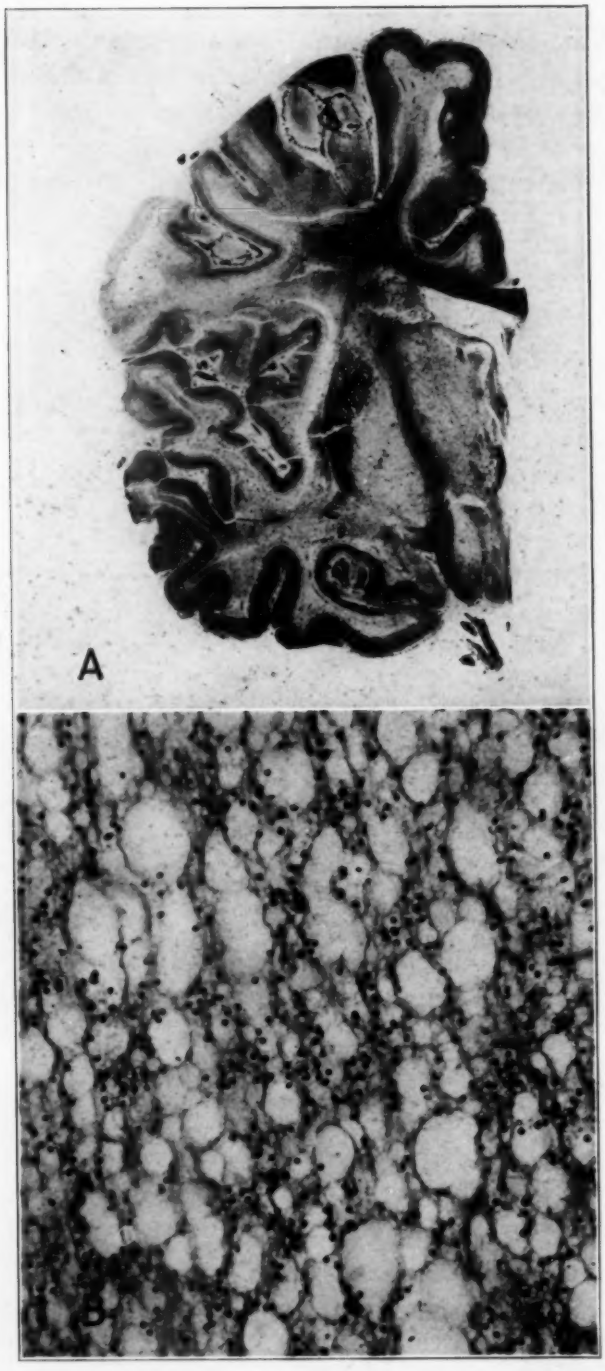

Fig. 18.—*A*. Coronal section of a hemisphere showing the extensive loss of myelin from the white substance. *B*. The spongy appearance of the subcortex. Nissl stain; × 160.

the process in his case was in the nature of a developmental aplasia rather than an inflammatory or degenerative disease. But it is rather difficult to conceive of a condition of maldevelopment or malformation in which the ganglion cells in the gray matter are normal and their axons are present, degenerating only on reaching the subcortical zone where only a few small collection of fibers remain undisturbed. The concep-

Fig. 19.—Character of glia cells, hypertrophied astrocytes (*A*) brought out by Cajal's gold-sublimate method (modified); × 360.

tion of aplasia of the myelin and the axis cylinders advanced by Merzbacher, apparently found its main support in his inability to demonstrate a well defined glial reaction. This, of course, he considered as strong evidence against the degenerative or inflammatory character of the morbid process. He recorded, however, the presence of glial proliferation in the thalamus. This would seem to indicate that while in this

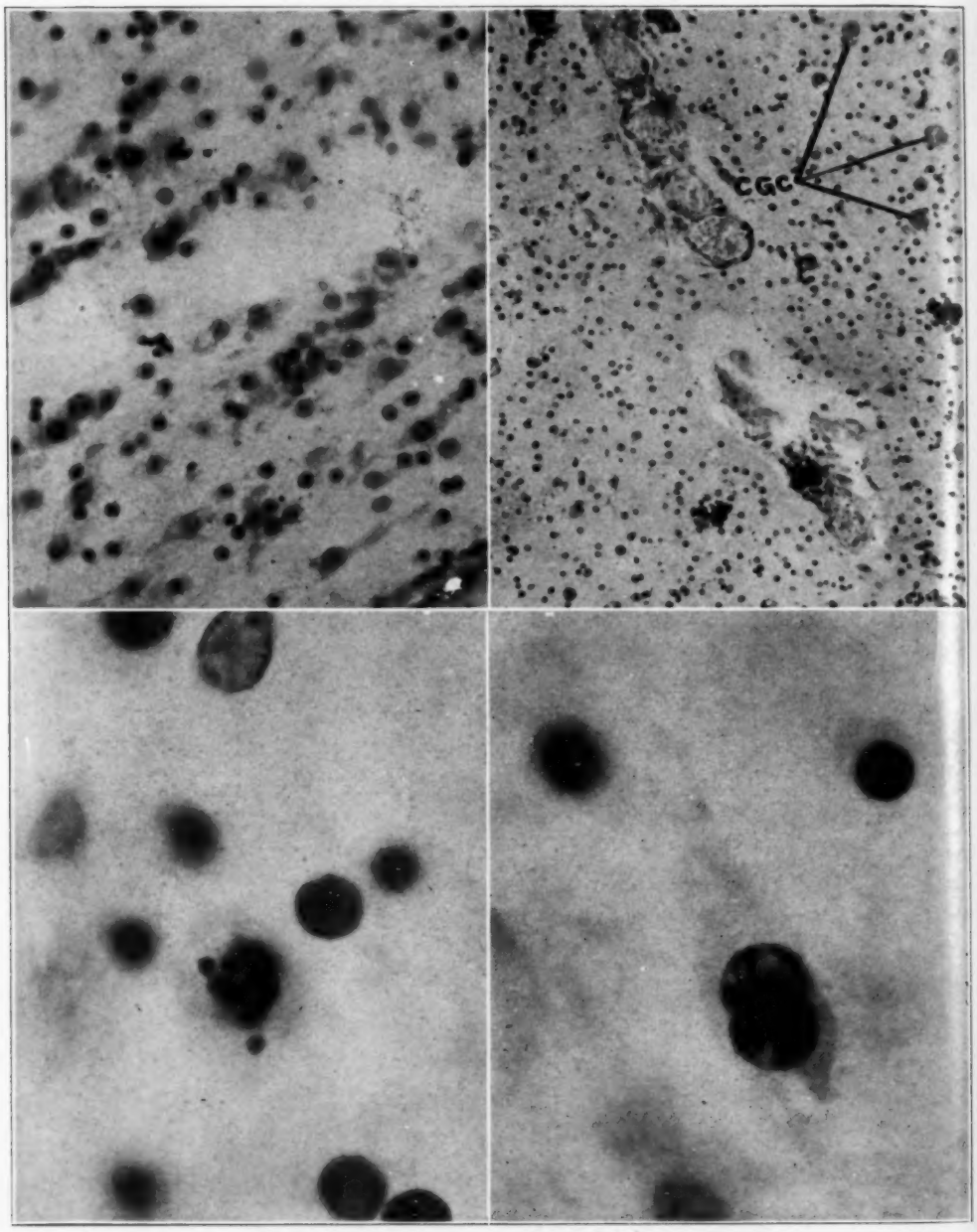

Fig. 20.—Fields in section in figure 18, under higher magnification (same staining method). *A*. Active glial proliferation; × 130. *B*. Degenerating compound granule cells (*C G C*); × 400. *C*. and *D*. Mitosis of glia cells; × 2,000.

structure there are disease changes still in progress, the process in other subcortical structures or regions has passed into a state so frequently observed in the final stages of the so-called sclerosis. He did not describe this condition of sclerosis, but one wonders what had taken the place of the destroyed or undeveloped axons and myelin sheaths if not some form of scar tissue; and since he definitely excluded productive or infiltrative mesodermal reactions, is one not forced to assume the presence of some glial tissue which for some reason did not respond

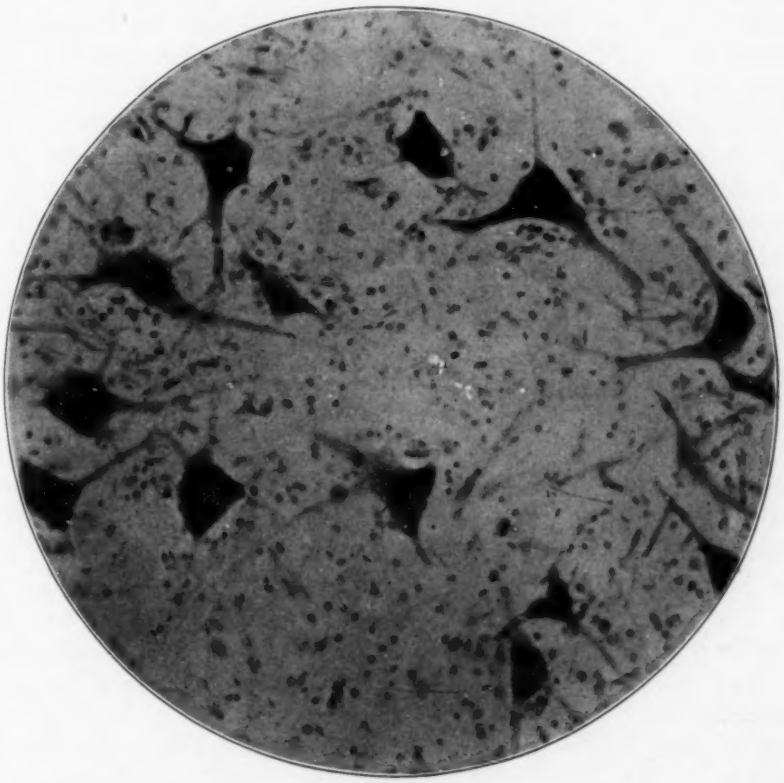

Fig. 21.—Normal nerve cells in brain stem. Nissl stain; × 160.

to the staining methods he employed? This may be the explanation particularly in view of our experience wtih the material in the first case when glial stains were obtained with difficulty and only on repeated attempts. Can one, therefore, with certainty exclude the possibility of a degenerative process being responsible for the pathologic picture in his case? The familial character of the disease does not militate against this conception—for, as will be noted, the cases of Krabbe which were distinctly degenerative in character were also familial in nature.

Schilder summed up the microscopic changes in the so-called encephalitis periaxialis diffusa by enumerating the following typical features: (1) sharp demarcation and limitation of the disease process to the white substance of the brain; (2) marked destruction of the myelin with an apparently secondary and less complete dissolution of the axis cylinders; (3) widespread and large accumulation of glial elements, including spider glia cells, fiber-forming astrocytes and compound granular cells, and (4) adventitial infiltrations mainly with compound granular cells (Koernchenzellen) and variable numbers of lymphocytes.

It is apparent that the histologic and topographic features as described by Schilder [11] are strikingly similar to those noted in our cases. From the name used by the author, however, it would seem that he regarded the disease process as inflammatory in nature, mainly because of the presence of mild adventitial lymphocytic infiltration among other and more dominant observations. In this regard, he is supported by a similar interpretation given by Neubürger,[16] who described two similar cases, in which he found adventitial lymphocytic infiltrations alongside distinctly degenerative lesions, and concluded that a primary inflammatory process is responsible for secondary though predominant degenerative changes.

It is evident that the observations of adventitial infiltration, no matter how rare and how small, serve as a determining factor in the decisions of the majority of the authors quoted in placing their cases among the encephalitides or inflammatory diseases of the brain. And this, in spite of the well known fact that lymphocytic infiltrations of blood vessels are frequently seen in manifestly noninflammatory lesions of the brain and spinal cord. They are common in neoplastic gliomatous invasions of the brain, in purely degenerative lesions such as encephalomalacia and also often in other degenerative disease forms such as multiple sclerosis and combined sclerosis. Bearing this in mind, may not these subordinate and secondary reactive mesodermal changes be disregarded and the selective dissolution of ectodermal elements be looked on as the primary lesion?

Indeed, it is also claimed that such changes as we have described could be regarded in the light of Lubarsch's definition of inflammation as essentially inflammatory. Lubarsch,[17] in his definition of inflammation, included any structural modification in which alterative, productive and exudative changes were jointly manifested.

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16. Neubürger, K.: Histologisches zur Frage der diffusen Hirnsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:336, 1921; Zur Histopathologie der multiplen Sklerose im Kindesalter, ibid. **76**:384, 1922.

17. Lubarsch: Pathologische Anatomie (L. Aschoff), ed. 6, Jena, Gustav Fischer, 1923, vol. 1, p. 514.

Under such a conception, however, a predominantly ectodermal structure undergoing a noninflammatory regressive process might, with the addition of a slight secondary mesodermal reaction, display all the features of an inflammatory process. While such an interpretation has good physiologic reasons, it nevertheless disregards the older division of morbid processes into inflammatory and degenerative. If one amalgamates into one process the dissolution of highly specialized tissues on one hand, and the constructive, productive responses of mesodermal derivatives on the other, one does away with a useful distinction between degenerative and inflammatory lesions. The latter not only are distinct from a morphogenic point of view but also relate to an important difference in the provocative or causative factors.

Krabbe's case 1, which stands in still closer relationship to our material, offers the most substantial support for our conception of a toxic origin and degenerative character. Its clinical picture is highly significant for its bearing on the nature of the anatomic observations and will be found in the review of other similar cases elsewhere in the article. The pathologic changes as summarized by Krabbe were: (1) limitation of the destructive changes to the white subcortical substance; (2) a form of perivascular myelin necrosis, characterized by destruction of myelinated fibers in the immediate vicinity of blood vessels, with the formation of wings of glial proliferation about these vessels; (3) less marked destruction of myelinated fibers in areas outside of the perivascular zones; (4) glial proliferation in the involved areas with formation of compound granular cells and other forms of glial elements, and (5) complete absence of mesodermal reaction of any form.

The strictly destructive change without any inflammatory reaction in his material led Krabbe to suggest the degenerative character and toxic origin of the disease. It was also his belief that the toxin, circulating in the blood stream, first attacked structures adjacent to the walls of blood vessels, since the process of dissolution and gliosis was most prominent in the vicinity of the vessels. He also felt that the so-called diffuse sclerosis may, in many instances, be the end-stage of the condition which he described under the name of perivascular myelin necrosis.

Thus, in his case there is an instance in which inflammatory changes are definitely ruled out by the absence of mesodermal reaction.

The condition in one of our cases (case 4) can be safely regarded as a parallel stage of a similar process, in which the degenerative changes are in the foreground, while the other three cases, cases 1, 2 and 3, represent older stages of the same general disease form.

In our case 4, as in Krabbe's case 1, it may be assumed that a toxic agent of some sort is probably responsible for the selective destruction of the myelin, the involvement of the axis cylinders being a secondary reaction. In other cases, it is probable that the glial and mesodermal elements reacted when the destructive process was well under way.

Krabbe, in his second group of cases,[18] found that in his material there was complete destruction of axis cylinders as well as of medullary sheaths with replacement by neuroglia, while the nerve cells were relatively intact. It was his belief that the process was gradually and uniformly unfolded, for the absence of cysts and the regularity in glial proliferation point against a sudden or showerlike occurrence. He thought that the even character of the gliosis and the lack of deformation of the brain was the result of a steady breaking down of brain tissue and a parallel substitution by glia. He argued against an inflammatory nature of the disease, and in support of its degenerative character, cited the strict limitation of the lesion to the white matter and the selective destruction of the processes of the cortical pyramidal cells. On recalling his first case of the so-called perivascular myelin-necrosis,[19] he withdrew his earlier conclusions with regard to its histogenesis. In that instance the destruction of medullary sheaths was predominant in close proximity to the blood vessels and less marked at the periphery. This he regarded as pointing to a perivascular origin of the process. But on reconsideration he assumed that the actual disease process was diffuse and uniform and was only apparently more intense around the blood vessels, because the phagocytes which had picked up products of destruction from wide zones were gathered more densely around the blood vessels. His final conclusion was that the disease was in the nature of a degenerative process and was analogous to such degenerative conditions as are seen in hereditary or familial diseases of the central nervous system, such for instance as Friedreich's heredo-ataxia. The latter interpretation he based on the selective character of the disease. Here it may be recalled that the study of one of us (Globus[20]), on amaurotic family idiocy, has yielded evidence in support of a primary disease of the white matter of the cerebrum and cerebellum.

In order to establish the nosologic position of his cases, Krabbe assembled a number of reports of similar cases recorded in the literature and attempted to subdivide them into three distinct groups: (1) syphilitic, (2) encephalitis periaxialis diffusa and (3) familial early infantile form of diffuse brain sclerosis (his own form).

With the first group we are not concerned, because in none of the cases reviewed for this paper was a syphilitic etiology proved. Krabbe himself found it difficult to establish such a group.

Into group 2, he admitted mainly those cases that were reported under the term of Schilder's disease. He was inclined to regard the

18. Krabbe (footnote 12, second reference).

19. Krabbe (footnote 12, first reference).

20. Globus, J. H.: Ein Beitrag zur Histopathologie der amaurotischen Idiotie, Ztschr. f. ges. Neurol. u. Psychiat **85**:424, 1923.

latter as a form of diffuse disseminated sclerosis. He reserved group 3 for his own material, which he believed to constitute a disease entity. He defined it as a familial, early infantile form of diffuse brain sclerosis. It differed greatly from Schilder's disease, for the latter, in his opinion, was too circumscribed, was probably in many instances mainly a reparative inflammatory process, developed in later infancy and had no familial features. He was aware of Haberfeldt and Spiller's case,[21] but had some doubt of its familial character, not being willing to accept the parents' interpretation of the malady which occurred in the other members of the family.

Krabbe found a close relationship between his cases and those described as the Merzbacher and Pelizäus disease, because of the clinical similarity, its occurrence during the first years of life and the pronounced destruction of the white matter, but differing somewhat from it in that the clinical course in some of the cases of Merzbacher's disease remained stationary. With amaurotic family idiocy he found similarity in the progressive and fatal course of a familial degenerative disease.

Bauman [22] also attempted an analysis of the clinical and anatomic features of the cases recorded in the literature, and, following the lead of Krabbe, established three types: inflammatory, degenerative and neoplastic. Among those considered as inflammatory there is only one, the case of Siemerling and Kreutzfeldt,[23] which falls into our group, and we regard it as degenerative for reasons given elsewhere. In the degenerative class he had a larger number of acceptable cases. In his third class of neoplastic gliosis, he mentioned the case of Ceni,[24] which we, in accord with Schilder, believe to be degenerative.

Before concluding the discussion of the microscopic features of the disease, we are tempted to recall Virchow's [25] observations on a disease process, which he termed congenital interstitial encephalitis. He found in the brains of infants and young children who died under rather obscure circumstances an enormous increase of glia cells, which were hypertrophied and crowded with fat granules (compound granular cells). With the progress of the disease, those cells showed further and more intense change. They lost their outline and frequently took

21. Haberfeldt, W., and Spiller, F.: Zur diffusen Hirn-Rueckenmarks-sklerose im Kindesalter, Deutsche Ztschr. f. Nervenh. **40**:436, 1910.

22. Bauman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:453, 1924.

23. Siemerling, E., and Kreutzfeldt, H. G.: Bronzekrankheit und sklerosierende Encephalo-Myelitis, Arch. f. Psychiat. **68**:217, 1923.

24. Ceni, C.: Ueber einen interessanten Fall gliomatoeser Infiltration beider Grosshirnhemispheren, Arch. f. Psychiat. **31**:809, 1898-1899.

25. Virchow, R.: Kongenitale Encephalitis und Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867; Ueber interstielle Encephalitis, ibid. **44**:472, 1868.

the form of irregular lumps of fat granules embedded in a peculiar hyaline substance (fig. 3). These granular cells were found principally in the white substance of the brain, while the gray substance was free from them or showed only slight changes. He interpreted these observations as indicative of an inflammatory process, and suggested the probability of a prenatal, interstitial encephalitis, the disease having been transmitted by the mother, who may have suffered from some infection during gestation.

He was subsequently confronted by the observations of Jastrowitz,[26] who studied a large number of brains of infants who had died from various causes during the first five months of life. He found large numbers of diffusely scattered compound granular cells in such brains. He considered them as an expression of a normal physiologic phenomenon in the process of building up the brain tissue, as well as in the course of the disposal of waste products of a normal brain. The question concerning the significance of an excessive number of granular cells was left unanswered by him, though he suggested that wasting diseases and malformations in the central nervous system lead to an increase in these phagocytic elements. His studies do not deprive Virchow's observations of their significance, and it is possible that Virchow's material included instances of diffuse degenerative disease not unlike that seen in our group, but unfortunately his studies were mainly pathologic and did not include clinical observation.

GENERAL CLINICAL CONSIDERATIONS

While the object of this paper is to discuss mainly the pathologic relationship of this group of cases, it will not be fully attained unless it is accompanied by a survey of their clinical features. Indeed, a study of the individual clinical histories does not yield a definite clinical picture that could be safely regarded as pathognomonic for the entire group. As a matter of fact, the pathologic observations, though limited to the white matter, are of such a diffuse character that diverse signs and symptoms would be expected.

On the other hand, the clinical manifestations, such as those described by Heubner [27] for diffuse sclerosis and those by Merzbacher, Schilder, Krabbe, Schminke,[28] Hermel, Collier and Greenfield [29]

26. Jastrowitz, M.: Encephalitis und Myelitis des ersten Kindesalters, Arch. f. Psychiat. **2**:389, 1869-1870; ibid. **3**:162, 1871-1872.

27. Heubner, O.: Ueber diffuse Hirnsklerose, Charité-Ann. **22**:298, 1897.

28. Schminke, A.: Encephalitis interstitialis Virchows mit Gliose und Verkalkung, zugleich ein Beitrag zur Varkalkung intrazerebraler Gefaesse, Ztschr. f. d. ges. Neurol. u. Psychiat. **60**:290, 1920.

29. Collier, J., and Greenfield, J. G.: The Encephalitis Periaxialis of Schilder, a Clinical and Pathological Study, with an Account of Two Cases, one of which was Diagnosed During Life, Brain **47**:49, 1924.

and others, justify the creation of a new clinical group. Thus an abrupt onset, a rather rapidly progressive course, characterized by mental deterioration, rapidly advancing spastic paralysis, epileptiform attacks, features of decerebrate rigidity, ocular palsies and other ocular manifestations such as nystagmus, optic atrophy and blindness without optic atrophy followed by a rapid decline with fatal issue (within two years) are features fairly typical.

This conception of the clinical and pathologic nature of this disease is the result of the study of our material and a careful survey of a number of similar clinical and pathologic studies, particularly those which have been reported under the heading of encephalitis pariaxialis diffusa. They had to be scrutinized with particular care, since no two authors reviewing this material are in full agreement concerning the merits of many of the cases reported under this name. The main reason for this disagreement is probably explained by variations in the interpretation of the term created by Schilder. Schilder himself may be held responsible for this misunderstanding, for in a second contribution made by him to this subject he gave a more liberal interpretation to his first definition of the disease, permitting the inclusion of instances only remotely resembling the first case, which is set up as the type. Thus, it is essential that the term encephalitis periaxialis diffusa be first clearly defined, and only then should an attempt be made to regroup material in accordance with the clear understanding of the character of the disease and the limitation of the term.

In his first contribution, Schilder defined the disease in the following way: "It is a diffuse disease of the white matter of the hemispheres, occurring in childhood and which, because of characteristic macroscopic and microscopic findings, may be regarded as a disease entity." The clinical picture of this disease, he stated, is exceedingly variable; it may run the course of a tumor of the brain or acquire the picture of multiple sclerosis and then again may simulate the diffuse sclerosis of Heubner.[27] It may be suspected when symptoms point to a diffuse lesion involving both hemispheres, or in instances in which the disease runs a rapid clinical course not unlike that of multiple sclerosis of the young. The disease is fatal and there is but a slight tendency for remission. He also added that it is related pathogenetically to multiple sclerosis and, particularly, to its acute form. It bears no relationship to pseudosclerosis, tuberous sclerosis and a number of forms of the so-called diffuse sclerosis. A toxic factor is probable, but the etiology is still unclear; it is also probable that endogenous factors contribute to its development. The conception of a peculiar predisposition of the brain lacks morphologic evidence in its favor.

Thus, with Schilder's definition as a guide, it becomes apparent that there are a number of cases which have been erroneously grouped under this term and which on reconsideration must be excluded. The exclusion of these cases is determined first by the age of the patients, second by some of the clinical features such as the occurrence of protracted remissions and third by the lack of typical gross and microscopic alterations. While it is true that a similar process may exist also in older persons, nevertheless, it is dangerous to include such cases in this group, since it might lead to the error of grouping together a large number of somewhat similar disease forms which could to better advantage be classed with multiple sclerosis. The need of guarding against this error is obvious when it is recalled how difficult it is to distinguish the changes in the disease under discussion from those of multiple sclerosis. If progress is to be made in the recognition of the true nature of this disease, one must limit oneself to material from cases characterized by a specific clinical picture and associated with uniform morphologic alterations.

With this in mind, we have selected a number of instances from the literature which may be regarded as within the meaning of the title of this paper. It is furthermore suggested that by introducing the term "progressive degenerative subcortical encephalopathy" in place of "encephalitis periaxialis diffusa" we are describing the condition more correctly.

In the following pages, we submit brief abstracts from the clinical histories and postmortem descriptions of the cases which have many clinical and anatomic features in common with those of our group. The cases are arranged in the chronological order of their appearance and the descriptions are followed by a few remarks in which we give our interpretation of their anatomic features.

CASES REPORTED IN THE LITERATURE

CASE 1 (Heubner, 1897).—A boy, aged 4½ years, showed delay in learning to speak; otherwise development was normal. The onset of the illness was sudden and was ushered in by repeated attacks of vomiting and difficulty in swallowing. This was followed by progressive mental deterioration, gradual development of spastic quadriplegia and early bilateral optic atrophy. Toward the termination of the illness there were further impairment of speech, marked contractures, tremors, exaggerated deep reflexes and absent abdominal reflexes.

The anatomic observations were made only on gross material and were summed up as diffuse sclerosis of the brain and spinal cord.

CASE 2 (Ceni, 1898).—A girl, aged 9 years, had a somewhat insidious onset, ushered in by progressive clouding of the intellect; this was followed by mental deterioration, by the appearance of bilateral pyramidal tract signs, right facial paralysis, tremor in the right arm, unsteady gait and progressive loss of vision. Within several months, total blindness, bilateral temporal pallor of the disks, scanning speech and ataxia of both arms developed. The course was rapidly

progressive. She developed incontinence, paralysis and contractures in all extremities and died at the end of seven months of illness.

There was a diffuse gelatinous sclerosis of the white substance, particularly in the left hemisphere. Ceni's histologic study led him to regard the disease process as neoplastic, but his observations are not convincing, and we, in accord with Schilder and others, are inclined to regard the anatomic alteration in the nature of a degenerative lesion, similar to that found in our group.

Case 3 (Haberfeldt and Spiller case, 1910).—A girl, aged 7 years, the second child in the family to die of the same disease, had an illness that was ushered in by failing vision and gradual intellectual deterioration. She became apathetic and dull. A progressive decline was marked by complete blindness, aphasia, further mental deterioration, spasticity in the lower extremities and muscle spasms. Death occurred two years after the onset.

The anatomic observations were typical in the white matter of the cerebral hemispheres, but some changes were also reported in the cerebral cortex. The latter were described as shrinkage and loss of the large pyramidal cells and moderate gliosis. Schilder, on restudying the case, accepted the subcortical changes as typical of his disease but was unable to verify the observations on the gray matter, for lack of material. It is, however, often the experience of neuropathologists to see such alterations in the cortex to which they assign little significance, for it is felt that unless such alterations are associated with well defined reactive phenomena they cannot be accepted as significant morphologic changes.

Case 4 (Schilder, 1912).—A girl, aged 14, had an illness with an onset marked by impairment of vision and gradual mental deterioration. It was followed by attacks of vomiting, headaches and slight papilledema. Vision was soon completely lost, but the pupillary reactions remained intact. There soon appeared right hemiplegia and aphasia, which were followed by complete loss of mentality. The patient died five and one-half months after the onset.

The pathologic observations were in the nature of demyelination and gliosis in both occipital lobes, extending forward to the left temporal lobe, but less so in the right hemisphere. In describing his observations, Schilder stressed the normal consistency and unchanged configuration of the brain, and the sharp limitation of the disease process to the subcortex. He also emphasized the relative preservation of the axis cylinders in spite of the hyperplasia of fiber-forming astrocytes, the nuclei of which showed variations in size and number. Compound granular cells were also found in large numbers. There were only a few lymphocytes.

Case 5 (Krabbe, 1913).—A child, aged 1 year, who had been perfectly well, became suddenly ill. The acute onset manifested itself in diarrhea, followed by obstipation, rise in temperature and semistupor. In the final stage of the illness, which developed rapidly, repeated epileptiform attacks occurred, associated with tonic contractures, opisthotonos and ocular palsies. Death occurred eight days after the abrupt onset of the illness.

The pathologic changes were: (1) limitation of the destructive changes to the white, subcortical substance; (2) a form of perivascular myelin necrosis, characterized by the destruction of myelinated fibers in the direct vicinity of the blood vessels and by the formation of rings of glial proliferation about these vessels; (3) less marked destruction of myelinated fibers in areas outside of these perivascular zones; (4) glial proliferation in the involved areas with formation of compound granular cells and other forms of glial elements, and (5) complete absence of mesodermal reaction of any form—infiltrative or productive.

This case, which bears a close resemblance to our case 4 is of significance because of its acute course, and hence the presence of morphologic features characteristic of the early stages in the pathologic process.

Case 6 (Krabbe, 1916).—A boy, aged 13 months, who had developed normally up to the age of 5 months, became acutely ill. He began to cry frequently and convulsively and developed rigidity of all the extremities. The arms assumed an obstetric posture and the legs became crossed. Three months later, he displayed only a few positive neurologic observations. There was early optic atrophy. During the examination he cried and gasped violently, and the body and limbs became stiffly extended, with the head retracted, hands clenched, sometimes in tetanic posture, while the lower extremities became strangely extended and adducted and the toes spread. There was a bilateral Babinski sign. During the next six months, he showed mild remissions, but toward the end there was a progressive decline, the spasticity became intensified and tonic spasms became more frequent, and easily provoked by slight stimulation, even by loud speaking.

The brain was reduced in size; its consistency was increased. This was less pronounced in the cerebellum and medulla. Microscopically, it showed diffuse demyelination and diffuse gliosis in the white matter. The gray substance was intact.

Case 7 (Krabbe, 1916).—A girl, a sister of patient 2, had a normal birth at full term. It was noticed early, however, that the child was unusually stiff. At the age of 4 months she developed frequent fits of vomiting and crying spells, which disappeared when the patient was put on a modified diet. It was soon noticed that the child did not advance mentally and that the rigidity of the neck and legs continued. At the age of 9 months she appeared rather stupid. She would cry often and convulsively. There was marked opisthotonos, unusual rigidity of the muscles, mainly in the lower extremities. The latter were hyperextended and adducted. The hands and feet were in tetanic posture. The right optic disk was atrophic, and the left was pale. There was a steady decline, and toward the end she was unable to swallow. She died after a period of unconsciousness.

The brain was of increased consistency; the gyri were unusually small and slender. The cranial nerves were hard and thickened. The cortex was of normal appearance, but the white matter was exceedingly hard and of a peculiar grayish translucent color. Microscopically, the cortex was intact, although changes, which are described as chronic inflammatory changes of the ganglion cells, were noted without glial reactions or perivascular infiltrations. The white matter showed changes similar to those in case 2, except that more fat accumulations were found in the scavenger cells. Here also the changes in the gray matter were not regarded as true morphologic alterations.

Case 8 (Krabbe, 1916).—A girl, who had had a convergent squint from early infancy was otherwise normal up to the age of 5 months, when she was taken acutely ill with diarrhea. A week later, stiffness of the body with opisthotonos and violent crying spells developed. One month later, the following signs were observed: convergent strabismus, generalized rigidity, opisthotonos, nystagmus in both eyes, flexion contractures at the elbow joints, clenched fists and extended and rigid lower extremities. There was a rapid decline with numerous convulsive attacks merging into a state of permanent rigidity. Finally, she was unable to swallow and died at the age of 8 months.

The ventricles were markedly dilated, with the brain greatly reduced in size. The cerebellum was extremely hard. Microscopic observations were not recorded.

Case 9 (Krabbe, 1916).—A girl, aged 11½ months, a younger sister to the patient in case 4, had a clinical course similar to that in case 3. She was normal during the first months of life, but later gradually developed rigidity of the extremities and tonic spasms. She died at the age of 1½ years.

The brain and spinal cord were of normal form, but were exceedingly hard, particularly in the white matter, which showed marked destructive changes and dense gliosis.

Case 10 (Krabbe 1916).—A boy, was well up to the age of 4 months, at which time he began to suffer with constipation. Shortly afterward he developed attacks of screaming and tetanic rigidity of the upper and lower extremities. He developed peculiar movements of the mouth and tongue. At the age of 7 months, he displayed transient nystagmus, retraction of the head and contractures. The hands were firmly clenched, the arms were in rigid flexion at the elbow, the legs stiffly extended at the knees and adducted at the hip joints and the feet were in equinus posture. He displayed periodic attacks of marked tonic rigidity. He declined slowly but steadily. Toward the end the disks became somewhat pale; he was unable to swallow and died at the age of 11½ months.

The brain was small, of normal shape and of hard consistency. An increase in glia was reported, although microscopic studies were not recorded.

Case 11 (Schroeder, 1918).—A boy, aged 12, had had an acute onset with loss of sphincteric control and progressive mental deterioration, followed by spastic diplegia and the appearance of contractures. The duration of the illness was two and one-half years.

Diffuse symmetrical sclerosis, demyelination, relative preservation of the axis cylinders and mild perivascular infiltrations were present. The case was regarded by Schroeder [30] and later also by others (Bauman) as an instance of encephalitis mainly because of the presence of a mild mesodermal reaction. This is not in accord with our views as already discussed in the text.

Case 12 (Schmincke [28]).—A child, aged 9 months, developed a peculiar stiffness in all the extremities, frequent attacks of vomiting, rise of temperature and general restlessness a few days after birth. The child was thought to have been infected by the mother, who had had influenza. The child cried loudly, as if in pain, especially when touched. With the cry, all the extensor muscles of the body were drawn into spasms, the head was held stiffly backward, the legs stretched out, the fingers flexed and the hands were spastic and clenched. There was marked lordosis. This position was assumed rapidly during examination and appeared as an intermittent extension spasm. When the child was on his back, the head was held stiffly to the right, the eyes turning in the same direction. The deep reflexes were exaggerated. The course of the illness was rather brief. The child died suddenly with terminal pneumonia.

The brain was exceedingly hard; it could be cut only with difficulty. The white matter was pearly white, of markedly increased consistency and was distinct from that of the cortex, which was softer.

The microscopic study of the material showed the cerebral cortex to be uninvolved, though when stained with Sudan III, a slight increase in the fat-containing cells was noted. These cells, however, did not bear any relation to the blood vessels. The more striking morbid changes were found in the subcortical layers. There was a marked increase of glia of the compound granular, as well as the fiber-forming type. Areas of calcification were also noted. Occasionally leuko-

30. Schroeder, P.: Encephalitis und Myelitis, Monatschr. f. Psychiat. u. Neurol. **43**:146, 1918.

cytic infiltration of the walls of the blood vessels was present. In summarizing the case, Schmincke decided in favor of an inflammatory process caused by some noxious agent in the brain, which led to glial reaction and slight proliferative inflammatory change. He interpreted the finding of calcium deposit as being the result of the abnormal fat metabolism.

Case 13 (Hermel, 1921).—A boy, aged 3½ years, suddenly developed a condition of restlessness, and cried frequently. He lost his appetite and stopped talking. Three months later his gait became unsteady; he walked only on his toes, and then began to drag his legs. Finally he could not walk at all. With this, difficulty in deglutition, loss of sphincter control and a washed-out facial expression developed. The patient became unable to support his head. There were constant horizontal oscillations of the eyeballs. In the attempt to walk, he showed cross-legged progression. There was marked weakness of the extremities. He presented bilateral pyramidal tract signs. He declined progressively. More spasticity developed in the upper extremities, with flexure contractures at the elbow. Ataxia and incoordination of the upper extremities became marked. He was totally unable to walk and speech was completely lost. The child could hardly be fed, since it was impossible to open his mouth; stupor gradually developed and the child died.

The brain was reduced in consistency. The white matter of the hemispheres was the site of the pathologic process. Small cells with round pyknotic nuclei were found in large numbers, alternating with large bladder-like cells. In addition, there were numerous compound granular cells, free or in the perivascular spaces. Destruction of nerve fibers, extravasation of the blood and occasional new formation of capillaries and gliosis were marked. There was, however, no evidence of mesodermal reaction.

Hermel regarded the condition as a process of softening, with tendency to diffuse sclerosis, but differing from the latter by the existence of degeneration in the axis cylinders. He suggested the term "diffuse encephalomalacia chronica."

Case 14 (Neubürger, 1921).—A boy, aged 12, had a rapid onset of illness. At first there was incontinence which was followed by fixation of the pupils, and status epilepticus of jacksonian character.

Case 15 (Neubürger, 1921).—A girl, aged 4½, became acutely ill. At first weakness of the legs, crying spells and failing vision developed. The pupils and muscles of the eyes were intact. There was a progressive decline with a short remission. Toward the end there was marked rigidity of the extremities, pyramidal tract signs, impaired speech, retraction of the neck and laryngeal spasm. The duration of the illness was eighteen months.

The brain was small with symmetrical sclerosis of the white matter in both hemispheres, which invaded particularly the occipital lobes. The histologic changes were of the nature of areas of perivascular myelin necrosis. These areas fused into larger zones. The axis cylinders were destroyed less extensively. There was dense gliosis with many giant glia cells.

Case 16 (Siemerling and Kreutzfeldt, 1923).—A boy, age 7, had an acute onset, which was ushered in by restlessness, progressive impairment of speech, followed by unsteady gait. There soon developed spastic paralysis of the lower extremities and somewhat later spastic paralysis of the upper extremities. Bilateral pyramidal tract signs appeared. A single epileptiform attack occurred. Toward the end, difficulty in swallowing developed.

In addition to the typical lesions in the cerebrum there were similar lesions in the cerebellar hemispheres. Many rod cells and numerous compound granular

cells were found. They were inclined to regard this case as inflammatory, because of the mild mesodermal reaction, and thus suggested the term: sclerosing encephalomyelitis. They postulated a toxic or infectious agent attacking loci of more recent myelin formation.

Case 17 (Collier and Greenfeld, 1924).—A boy, aged 7, had an onset with convulsive attacks and progressive weakness of the legs. Three months later the patient was unable to walk. Convulsive attacks, jacksonian in character, appeared. The patient became dull, apathetic and apparently blind and deaf. He often cried out. He swallowed with difficulty. The head was retracted; the lower extremities became rigid and somewhat flexed at the hips and at the knees. He died nine months after the onset of the illness.

The brain was small; the gyri were atrophic; the white substance was replaced by pale, brownish, somewhat translucent substance of cartilaginous hardness. The gray matter was somewhat thinner in the affected area. The ventricles were dilated. There were no microscopic studies.

Case 18 (Collier and Greenfeld, 1924).—The gait of a girl became uncertain at the age of 4½ years, and vision was impaired. The vision failed progressively, but the pupils remained normal and the ocular movements intact. The lower extremities became slightly spastic and ataxic; the abdominal reflexes diminished and a bilateral Babinski sign appeared. There was a gradual progression. The patient became more and more rigid and was paralyzed in both the upper and the lower extremities; she deteriorated mentally and was aphasic and unable to swallow. The trunk was in opisthotonos with the lower extremities extended and adducted. The duration of the illness was fifteen months. The condition was diagnosed as Schilder's disease during the life of the patient. The anatomic observations were typical of this disease.

Case 19 (Flatau, 1925).—A boy, aged 14, had an onset that was somewhat insidious and was marked by impaired hearing. Four months later the sight became impaired. At the end of seven months, the patient was totally blind. At this time he experienced difficulty in walking and showed mental deterioration. There was a gradual decline leading to amentia and occasional convulsions. The duration of the illness was fourteen months.

There was diffuse gelatinous gliosis of the occipital and temporal lobes, which was restricted to the white matter. Hyperplasia of large astrocytes and accumulations of compound granular cells had developed in the diseased areas.

Case 20 (Brock, Carrol and Stevenson,[31] 1926).[32]—A boy, aged 8½ years, had an onset ushered in by irritability, restlessness, intention tremor in both hands and impairment of memory. A month later, impairment of vision, deafness and weakness in the right leg developed. There was a progressive change, and six months after onset, he passed through a generalized tonic and clonic convulsion which was followed later by mental deterioration and further impairment of vision. The course was slowly progressive at first and later gained momentum with the development of impairment of speech, right hemianopia, further mental deterioration, and spasticity of all the extremities associated with the features of decerebrate rigidity. He died fourteen months after the onset of the illness.

A diffuse subcortical gliosis involved mainly the occipital lobes. Mention was made of the presence of "typical" globoid cells, but from the illustration they appear strongly similar to compound granular cells.

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31. Brock, S.; Carrol, P. M., and Stevenson, L.: Encephalitis Periaxialis Diffusa of Schilder. Report of a Case, Arch. Neurol. & Psychiat. **15**:297 (March) 1926.

32. Cases 20, 21 and 22 have been added since this paper was read.

Case 21 (Steward, Greenfield and Blandy,[33] 1927).—A boy, aged 8, following the extraction of eighteen teeth, began to show a gradual decline in physical condition. About ten months later, he began to display mental alteration; he became dull and listless. Somewhat later, his hearing became impaired and his vision began to fail. This was followed by weakness in the legs. When examined eighteen months after the onset of the illness, he was blind, totally deaf and could hardly walk. From then on he declined more rapidly. He became incontinent; developed difficulty in swallowing, and the pupils became fixed. Intermittent, bilateral, primary optic atrophy, which varied in degree of nystagmus, and left sided hemiplegia developed. The clinical diagnosis was cerebral neoplasm.

Diffuse sclerosis of the white matter of the occipital and temporal lobes was present. There was a complete destruction of the myelin sheaths, less complete destruction of the axis cylinders, dense neuroglial overgrowth, large accumulation of compound granular cells and perivascular infiltration with mononuclear cells. The last feature, for want of a clearer description of the nature of the mononuclear cells, cannot be accepted as convincing evidence of an inflammatory process, and hence the case may be grouped with the degenerative instances of this disease.

Case 22 (Stewart, Greenfield and Blandy, 1927).—A girl, aged 3, became acutely ill. She developed attacks of gasping, vomiting and irritability, followed by drowsiness. The abdominal reflexes were lost, and there were recurrent Babinski signs. A month later, following a temporary remission during which she was able to sit up and even walk with support, there developed spasticity in the extremities and tremors in the hands, arms and jaw. She declined rapidly and died at the end of three months in a state of coma.

There was a symmetrical, brown, granular softening in the white matter of the parietal and occipital lobes with patches of demyelination in the pons. The histologic changes differed from those in their case 1 in that the gliosis took the character of a mild proliferation of the glial nuclei; there were only a few compound granular cells and no perivascular infiltration. The observations bear strong resemblance to those in our case 4, and it is possible that the marked necrobiosis with but scanty glial reaction is explained by the rapid clinical course.

SUMMARY

Personal observations on four cases and a survey of the clinical and anatomic observations in a series of twenty-two similar cases reported by other observers are presented. The outstanding anatomic features common to the entire group are the restriction of the pathologic alterations to the white substance of the cerebrospinal axis and the degenerative character of the lesion. The latter is in the nature of a diffuse demyelination and an equally widespread, though less complete, destruction of the axis cylinders with changes in the latter not unlike those seen in multiple sclerosis, combined sclerosis (progressive funicular myelopathy) and familial degenerative diseases such as amaurotic family idiocy (Globus[20]). As the parenchyma undergoes dissolution, it is replaced by diffuse glial hyperplasia and other glial alterations in which

33. Stewart, T.; Greenfield, J. G., and Blandy, M. A.: Encephalitis Periaxialis Diffusa. Report of Three Cases with Pathological Examinations, Brain **50**:1, 1927.

fibroblastic astrocytes and compound granular cells play a prominent rôle with the participation of microglia in its various modifications. The predominance of one or another type of glial element in these alterations is determined by the acute or chronic course of the lesion. In the more acute processes, the compound granular cells and the several forms of microglia predominate, while in the more chronic lesions the fibroblastic astrocytes form the bulk of the glial reaction. These variations in the character of the gliosis are obviously responsible for a corresponding variation in the consistency of the brain substance as noted on post-mortem examination of fresh material. The fibroblastic glia found in the more chronic lesions, of course, tends to increase the consistency of the brain, while the reverse is true of the more acute lesions, for in these the compound granular cells contribute to the appearance of softening. The lack of infiltration by mesodermal components is regarded as significant, for it points to the noninflammatory character of the disease. No less important is considered the diffuse distribution of the lesion and the absence of morphologic evidence of a constant locus which may be regarded as the primary seat. This is believed to have an important bearing on the clinical picture of the disease and to exclude the conception advanced by some observers that the sequence in which a given group of localizing signs and symptoms appear is to be regarded as characteristic of the onset and as diagnostic of the malady.

Obviously, while there is no set of signs and symptoms, the uniform occurrence of which in a given stage of the clinical course is to be regarded as pathognomonic of the disease, there is sufficient ground for the belief that the general clinical course and a few of the constant neurologic manifestations are highly suggestive and are of diagnostic value. Thus, a sudden onset of illness in the young, ushered in by some gastrointestinal disturbance, interrupted by a brief period of apparent recovery and followed by the development of a fairly typical chain of neurologic manifestations which unfold progressively and terminate in death, form a fairly well defined disease picture. The more constant of the neurologic manifestations are the progressive mental deterioration, the generalized rigidity, the advancing and spreading paralysis, the convulsive seizures and the rather infrequent episodes of decerebrate rigidity.

In regard to the pathogenesis of the disease, it seems probable that the abrupt development of symptoms indicates some sudden change in the normal metabolism in the central nervous system as though some toxic agent or endogenous poison had led to the arrest in normal differentiation and dissolution of the brain tissue. A defective anlage may be a contributive cause, but there is nothing in the morphologic features of the disease to prove its existence.

CONCLUSIONS

1. Progressive degenerative subcortical encephalopathy is the name suggested for a demyelinizing and sclerosing process in the brain of young children involving the white matter without involvement of the gray matter of the cerebral and cerebellar hemispheres.

2. The disease may be due to some toxic factor, of unknown nature, which affects the normal growth of the parenchymatous structures in the subcortical regions of the brain, causes their dissolution and results in proliferative glial changes.

3. Clinically it is characterized by a rather abrupt onset of illness, which often takes the character of a gastro-intestinal disturbance, and which, after a short period of apparent recovery, is followed by a series of generalized cerebral manifestations. Among the latter, mental dilapidation, spastic paralysis accompanied by advancing rigidity, contractures and convulsive seizures appear in varying sequence. Advancing blindness with or without optic atrophy, deafness and aphasia may develop at any stage of the illness, though most frequently early in the clinical course.

4. Some of the conditions described as chronic encephalomyelomalacia, diffuse sclerosis, perivascular myelin necrosis, encephalitis periaxialis diffusa, sclerosing encephaloleukopathia and interlobar symmetrical sclerosis should be grouped under the general name of progressive degenerative subcortical encephalopathy.

THE BRAIN IN MONGOLIAN IDIOCY

A REPORT OF TEN CASES *

LEO M. DAVIDOFF, M.D.
Peter Bent Brigham Hospital Fellowship Holder for 1926
NEW YORK

Mongolism, like acromegaly, exophthalmic goiter, cretinism and many other diseases deeply affecting the personality of its victims, may be diagnosed clinically at a glance. This fact gave rise to its quick recognition throughout the world after the name was coined by Langdon-Down [1] in 1866, and the literature became flooded with case reports and general articles on the subject. These, however, dealt with it largely from the clinical, statistical, sociologic and etiologic points of view.

The pathologic anatomy has received much less attention. This is especially true of the finer histology of the nervous system, and individual studies directed toward this point have usually been made on relatively few cases; moreover, the observations of various authors have often been contradictory.

The present report is based on a study of the brains from ten patients with mongolism found in the collection of the Staatskrankenanstalt-Friedrichsberg in Hamburg, and has been made possible by the kindness and help of Prof. A. Jakob, director of the laboratory. In the examination of these brains, special attention was paid to the histologic structure of the cerebral cortex, although, whenever possible, confirmation of the changes reported by other authors in other parts of the nervous system were sought.

REVIEW OF THE LITERATURE

In 1890, Wilmarth [2] briefly mentioned observations on five brains from mongolian idiots and called attention to the small size of the pons and cerebellum. Among the first to describe more completely the gross and microscopic status of the brains of patients with mongolian idiocy were Philippe and Oberthur [3] who, in 1901, reported two

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* From the Anatomic Laboratory of Prof. A. Jakob, Staatskrankenanstalt-Friedrichsberg, Hamburg, Germany.

1. Langdon-Down, J.: Observations on an Ethnic Classification of Idiots: Clinical Lectures and Reports, London Hospital, 1866, vol. 3, p. 259.

2. Wilmarth, A. W.: Report on an Examination of a Hundred Brains of Feebleminded, Alienist Neurol., 1890, p. 3.

3. Philippe, C., and Oberthur, J.: Recherches clin. et therap. sur l'épilepsie, Compte rendu du service des enfants idiots, épileptiques et arrières de Bicêtre **21**: 148, 1901.

cases. They found a rather vascular pia and a broadening of the upper cortical layers. The ganglion cells were properly alined in layers, but sometimes showed vacuoles in the protoplasm. They reported numerous embryonic elements among the nerve cells. Preparations with myelin sheath stains showed a reduction in the number of tangential and radial fibers in the cortex which, in part, also ran irregularly. The myelin of the white substance did not seem to show anything abnormal. The vessels were normal, aside from occasional simple sclerosis of the adventitia, sometimes with hyaline changes. Generally speaking, the changes were slight.

In 1903, Bourneville [4] published a report of one case in which the outstanding features were numerous meningo-encephalitic adhesions, underdeveloped convolutional structures and subnormal weight of the brain. It should be added that the patient died of generalized tuberculosis. That year also, Philippe and Oberthur [5] reported two cases in which the observations were even less divergent from normal than in the previous ones.

In his book on abnormal children, Shuttleworth [6] presented a picture of a brain from a child with mongolism. The cerebrum showed a markedly embryonic convolutional type; the convolutions were broad and thick, and secondary convolutions were largely absent. Multipolar cells are said to have been infrequent in the cortex. This simplicity of convolutional pattern was again pointed out by Bourneville and Reine Mangeret.[7] The embryonic convolutional type was again stressed by Comby [8] who also reported that he found few multipolar cells "as if some unknown cause has disturbed the development of the embryo in the first month of pregnancy."

Three more cases were reported by Oberthur [9] in 1904. In this report he stressed the presence of subacute and chronic changes in the nerve cells, neurophagocytosis, some meningeal and slight perivascular

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4. Bourneville: Idiotie du type mongolien; tuberculose pulmonaire, appendicite tuberculeuse, Recherches clin. et thérap. sur l'épilepsie, Compte rendu du service des enfants idiots, épileptiques et arrières de Bicêtre **23**:3, 1903.

5. Philippe, C., and Oberthur, J.: Examen histologique de deux cerveaux d'idiots mongoliens, Recherches clin. et thérap. sur l'épilepsie **23**:19, 1903.

6. Shuttleworth, G. E.: Abnormal Children from the Point of View of the Physician (French translation), Brussels, J. Lebêque et Cie, 1904.

7. Bourneville and Mangeret, R.: Nanisme mongolien, Recherches clin. et thérap. sur l'épilepsie **24**:149, 1904.

8. Comby, J.: Cas de mongolisme, Bull. Soc. d. hôp., Feb. 16, 1906.

9. Oberthur, J.: Examen histologique de trois cerveaux d'idiots du type mongolien, et du corps thyreoide de deux de cas malades, Recherches clin. et thérap. sur l'épilepsie **24**:169, 1904.

infiltration which were present in varying degrees in all three of his cases.

Vogt [10] summarized the pathologic anatomy of the brain in mongolism as reported in the literature as follows:

(1) Reduction in the weight of the brain (Wilmarth, Bourneville).

(2) Embryonic convolutional pattern (Shuttleworth, Biach, and especially Bourneville, Penell and others).

Microscopically: (1) Diffuse cortical changes (mild inflammatory reactions) affecting especially the frontal, posterior parietal, and calcarine areas (Philippe and Oberthur).

(2) Increased vascularization of the pia.

(3) Ganglion cells in the cortex in normal arrangement, but showing partial vacuolization in the protoplasm, neuroblasts.

(4) Glia not increased.

Biach [11] described the brain in a child, aged 6 months, with mongolism who died of pneumonia. Macroscopically, he found the cerebellum, pons and medulla smaller than normal. The cortical cells, especially in the frontal region, showed lack of differentiation with numerous double nucleated cells. The fourth layer appeared rich in cells; neuroblastic elements were numerous. The pia showed everywhere some infiltration with small round cells.

After a careful review of the literature, Weigandt [12] reported the pathologic changes in three brains from mongoloid children. He found in all what he believed to be an embryonic character of the ganglion cells, the cells being somewhat rounded with a noticeable number of light, large and small neuroblast-like elements present among them. He also found small collections of fat in some pyramidal cells and greater quantities about the blood vessels. These changes varied in degree, being striking in only one case. The third case, in which the patient was the least affected, as already described, showed, however, small patchy areas free from cells and other places rich in nuclear deposits around the vessels in which fat was also present. The author considered this as evidence of secondary degeneration in poorly developed cells, as often happens in other types of idiocy.

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10. Vogt, H.: Der Mongolismus, Vogt-Weigandt Ztschr. des jugend. Schwachsinns **1:** 445, 1907.

11. Biach, P.: Zur Kenntniss des Zentralnervensystems beim Mongolismus, Deutsche Ztschr. f. Nervenh. **37:** 7, 1909.

12. Weigandt, W.: Ueber Hirnrindenveränderung bei Mongolismus, Kretinismus, und Myxödem, Vogt-Weigandt Ztschr. des jugend. Schwachsinns **5:** 428, 1912.

More recent literature on mongolism has appeared in Holland. In a monograph, based on a study of 348 cases, van der Scheer [13] included a brief description of eighteen brains. He believed that the average weight of the brain is low for the age of the patients. He found that brains tended toward a spherical shape, with a shorter anteroposterior and longer lateral diameter. This, undoubtedly, is due to the usual brachycephaly. He also found the number of convolutions decreased and simple in form. The medulla and pons appeared strikingly small compared to the rest of the brain. In marked cases, the temporal poles lay close together across the midline, and the entire interpeduncular space and contents appeared to be hypoplastic; the author believed that the underdevelopment of important nerve centers in this region was responsible for the disturbances, so frequent in mongoloids, of the skin, mucous membranes, teeth, and lens of the eye, for the disturbances of sugar and fat metabolism and growth, and for the hypotonia and early death.

Gans,[14] who made the anatomic studies of van der Scheer's material, has published several brief reports in Dutch of his observations in these cases. In 1923, he wrote that among thirteen cases he found various anomalies of the cerebrum: the fossa sylvii was wide open in some, the frontal convolutions short, the gyri recti pointed, and an opercular form of the sulcus parieto-occipitalis was present in some. In one case he found a well developed taenia pontis; in another, thick aberrant fibrae arcuatae externae; in a third, in place of an elevation where the olive should be, a depression existed; on the other side, the whole half of the cerebellum was too small. The cerebellum in general was too light even in relation to the light cerebrum. The incisura posterior was usually wide, a condition obtaining also in the fetus. In one case, the accessory olives were small, the nuclei arcuati poorly developed and the olives small and poor in cells. The surface fibers of the pons were largely lacking, so that the pyramidal tracts lay almost on the surface of the pons. There were also much fewer pontile bundles passing through the pyramidal tracts and fewer covering them superiorly. The author expected to note that the lack was confined to neo-encephalic parts, but realized that the accessory olives, which were almost

13. Van der Scheer, W. M.: Beiträge zur Kenntnis der mongoloiden Missbildung (Mongolismus) auf Grund klinischer, statistischer, und anatomischer Untersuchungen (Die Bedeutung der Gebärmutterschleimhaut und des Amnions für die Ätiologie und Pathogenese dieser Missbildung), Berlin, S. Karger, 1927, pp. 162.

14. Gans, A.: De klinische en antomische onderzoekingen over de mongoloiede idiotie zyn de oorzaak dat het laboratorium in Sautpoort over 13 cerebra van lyders aan deze ziekte beschikt, Psychiat en Neurol. Bl., Amst., 1923, p. 301.

entirely absent, are among the oldest structures phylogenetically; the olives were relatively better preserved.

In 1925,[15] Gans described a peculiar formation in four cases of mongolism which he named "tuber flocculi." This consisted of a mixture of cerebellar elements—molecular and granular layers, and a certain number of Purkinje cells—all intermingled in a chaotic mass and located on the medial side of the flocculus. These nodules measured up to 5 mm. in length and 2.5 mm. in width; they were visible macroscopically. Well formed myelin radiations were not seen passing through the nodules, although occasional bundles of myelin fibers were noticed. The author considered that this structure was a cerebellar heterotopy. He had seen it in a case of congenital myoclonus, and believed it was a normal formation in the chimpanzee and orang-utan,[16] for he had observed it in both these apes although he had not had the opportunity to examine the areas microscopically.

This worker[17] also reported the absence of the striae (acusticae) Piccolomini in four cases of adult mongolian idiocy. These striae, as is known, arise in the nuclei arcuati, which in these four cases were also lacking. Since the author admits that in 10 per cent of normal human beings the striae Piccolomini are absent, however, and since, in practically all, they are not demonstrable until the age of 2, this observation cannot be of great value as specific to mongolism, particularly since many mongolian idiots die at an early age.

Gans[18] also found in three cases what he considered an incompletely differentiated calcarine cortex with corresponding defects in the laminae medullares of the corpora quadrigemina externa. This led him to speculate whether they have regressed to the state of mammals whose eyes are placed laterally.

It is evident from this review that the abnormalities in the nervous system in mongolian idiocy are numerous and extremely varied. Indeed, many of the changes stressed by some authors are absent in the reports of others. Among the pathologic observations that are common to the majority of cases, however, are the underweight of the brain, the relatively small size of the cerebellum and brain stem, the unusual

15. Gans, A.: Anatomische Bevindingen bij de Mongoloiede Idiotie, Nederl. Tijdschr. v. Geneesk., 1925, vol. 69, no. 8.

16. Since writing this article, I have had an opportunity to examine serial sections from the cerebellum in the collection of the New York State Psychiatric Institute from both these apes without finding any evidence of such a structure.

17. Gans, A.: Het outbreken der striae (acusticae) Piccolomini bij de Mongoloiede Idiote. Demonstratie no. 3, Psychiat. en Neurol. Bl., 1926, no. 2 and 3, p. 3.

18. Gans, A.: Anatomische Bevindingen bij de Mongoloiede Idiote: III. Afwijkingen in het centrale optische stelsel, Nederl. Tijdschr. v. Geneesk. **70**:4, 1926.

spherical form of the cerebrum and the embryologic simplicity of the convolutional pattern. The various reports of inflammatory changes in the pia and elsewhere must be regarded with some caution, as many mongoloid children die of generalized tuberculosis, which may be responsible for cellular infiltration in the pia and around the blood vessels, even though tubercle bacilli are not demonstrable.

I was unable to confirm the presence of the neuroblast-like elements described by several investigators. In all ten of my cases the size and appearance of the nerve cells, the development of the Nissl bodies and the number of dendritic processes were all in keeping with the standards accepted as normal for mature nerve cells in the various parts of the nervous system.

The studies made in Holland emphasize the developmental errors in the nervous system which are believed to be part of the general disturbance of development. Many of the anomalies described by van der Scheer and Gans were also present in my cases, but none was demonstrable with any degree of regularity. Van der Scheer's impression that the hypothalmic region is hypoplastic was apparently based on macroscopic observation only. The apparent underdevelopment of this region in the brains of mongolian idiots is readily understood from the fact that the temporal poles are usually so close together, owing, no doubt, as van der Scheer himself believes, to the brachycephaly.

MATERIAL AND METHODS

The material on which my investigation is based consists of the brains alone from ten patients with mongolian idiocy. The patients varied in age, at the time of death, from 7 months to 42 years. Another case was available but was discarded because the patient had died of tuberculosis, and the brain showed tuberculous lesions. One of the brains from a child, aged 7 months, showed a unilateral porencephaly. These brains had been contributed from various institutions at different times, and were incomplete in two cases, although enough material remained for thorough examination. In all of them the clinical picture had been so typical that no question could be raised about the diagnosis. The histories, on the other hand, were usually incomplete, and, in several of the cases, unavailable beyond a few bare facts.

The brains were photographed and weighed whenever fresh material was available. After the brains were weighed as a whole, the cerebral hemispheres and the cerebellum joined to the brain stem were weighed separately. One half of each brain was then fixed in formaldehyde and the other half in alcohol. From the material in formaldehyde, myelin sheath and fat stains were made, and frozen sections were cut from representative parts of the brain for Bielschowsky's silver method for neurofibrils. Large sections were then put into Müller's fluid and embedded for myelin sheath preparations. The material fixed in alcohol was embedded in celloidin, and the following stains were made: Nissl's toluidine blue, hematoxylin and eosin, van Gieson's stain for connective tissue, Victoria blue for glial fibrils and Turnbull's blue reaction for iron.

The report of the cases follows. Only a few will be presented in detail; the rest will be given briefly to indicate the important observations.

REPORT OF CASES

CASE 1.—*Mongolian idiot; eczema, marasmus, death from pneumonia. Brain underweight, embryologic convolutional pattern, generalized poverty of cells in the third cortical layer. Microscopic periventricular areas of degeneration.*

Clinical History.—An infant, aged 11 months, was the third living child. The mother had had two spontaneous abortions. She is said to have had syphilis, although this was not proved serologically. The child was born normally at full term and weighed 3,500 Gm. She was breast fed for only six weeks. After that, feeding according to various formulas was carried out artifically without successfully meeting the problem of nutrition. The child failed to develop mentally, was markedly undernourished and developed eczema. She was admitted to the hospital at the age of 3 months. The child was marantic, extremely sick and was not expected to recover. A Wassermann test of the blood, and tuberculin tests were negative. The mongolian features were noted only after several months. As the nutrition improved, the child continued to show marked hypotonia; the slanting eyes and protruding tongue became more evident; mental development was extremely backward. At the age of 8 months, in association with pharyngitis and bronchitis, the patient again lost weight rapidly. From then on the condition gradually grew worse; she died of pneumonia at the age of 11 months.

At necropsy, aside from extensive pneumonia, nothing beyond marked malnutrition was found in the body generally.

Brain.—The brain was distinctly small. The relatively short anteroposterior and broad lateral dimensions may be noted in the brain on the left in figure 1 which is more evident when compared with the brain of a normal infant (fig. 1, right). The photograph also shows well the marked proximity of the temporal poles to each other in the mongoloid brain, and the apparent underdevelopment of the hypothalamic region. The increased breadth and simplicity of the convolutions and the absence of secondary gyri are clearly seen when compared to the intricate convolutional pattern of the normal brain.

The entire brain weighed only 650 Gm. (The normal weight of a child's brain at the age of 11 months is about 825 Gm.[19]) Small as this may seem, the weight of the cerebellum and brain stem was even smaller. Their combined weight of 70 Gm. makes a ratio with the brain as a whole of about 1:9 as compared with 1:7, the accepted ratio in normal brains.

The meninges were normal. There were no abnormalities of the cerebral blood vessels.

Microscopic Examination.—The relative, as well as absolute, smallness of the brain stem and cerebellum, especially in view of Gans' observations of various congenital defects in this region in his cases of mongolism, led me to examine these areas first. No demonstrable changes, however, could be found microscopically in this case. The olivary systems did not show evident loss of ganglion cells or pathologic change of these elements. The nuclei arcuati were present and appeared normal. The cranial nerve nuclei were equally unaffected. The pontile nuclei and fibers seemed normal in appearance and number. The intracerebellar nuclei also were normal. The cerebellum itself did not show any abnormalities in Purkinje cells, molecular, or granular layers.

Since, in this particular case, the apparent hypoplasia of the subthalamic region, described by van der Scheer on gross appearance, seemed more marked than in

19. Von Bischoff, T. L. W.: Das Hirngewicht des Menschen, Bonn. P. Neusser, 1880, p. 171.

the other cases, this whole region, including the basal ganglia and lower portions of the thalamus from one half of the brain, was sectioned serially. No evidence of actual defects could be found. All the nuclei of the hypothalamus and tuber cinereum could be identified, and none showed any apparent scarcity of cells. Dr. Josephy, who has had much experience with the normal structure of this region, was kind enough to examine my sections and confirmed my opinion. The striate body, the thalamus, substantia nigra, body of Luys, and red nucleus all seemed unimpaired in their cell quotas and in their cytologic integrity.

Examination of sections from all parts of the cerebral cortex showed a normal pia and normal blood vessels. There was no sign of cellular infiltration or gliosis. The nerve cells seemed well formed and did not show disturbances of the Nissl

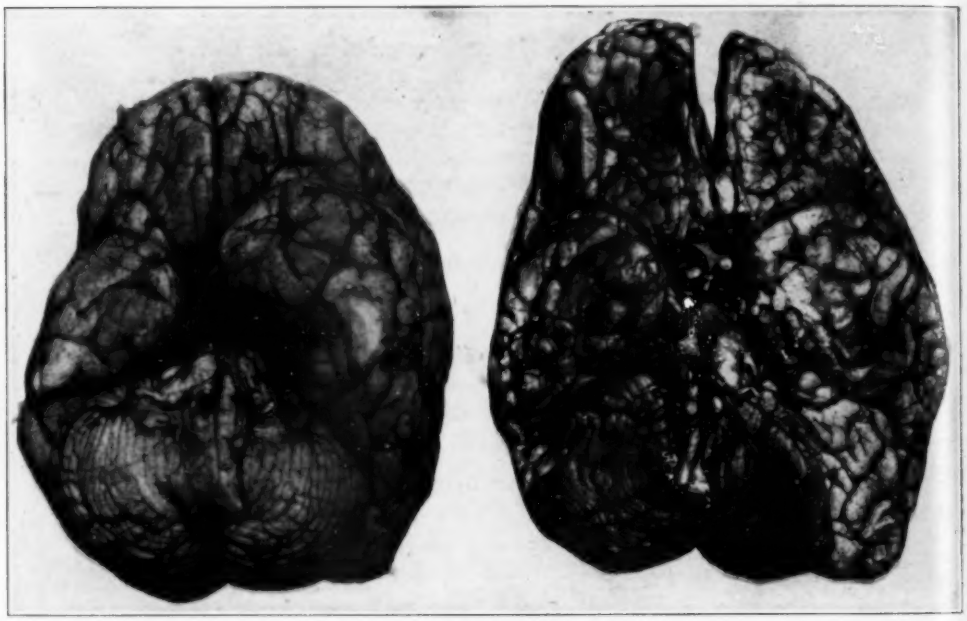

Fig. 1.—The figure on the left from case 1 shows embryonic simplicity of convolutions and close proximity of temporal poles to each other; reduced one-third. The figure on the right shows the brain from a normal infant of the same age as the patient in case 1; reduced almost one-half.

bodies or nuclei. The polarity and architectural arrangement of the cells were unimpaired.

A striking feature of all sections from the cortex was a distinctly small number of ganglion cells in the third cortical layer. This was nowhere accompanied by evidence of recent or remote destruction in the cortex itself. The picture in each case was that of an undisturbed cortical area, lacking merely in a certain number of cells which exist in the corresponding layer of the normal brain. This paucity of cells, while affecting the third layer for the greater part, was by no means confined to it; indeed it sometimes involved all layers. In figure 2 *C* of the parietal region it may be seen that the third layer alone is largely affected, while in figure 2 *A*, representing the anterior central convolution, nearly all layers seem

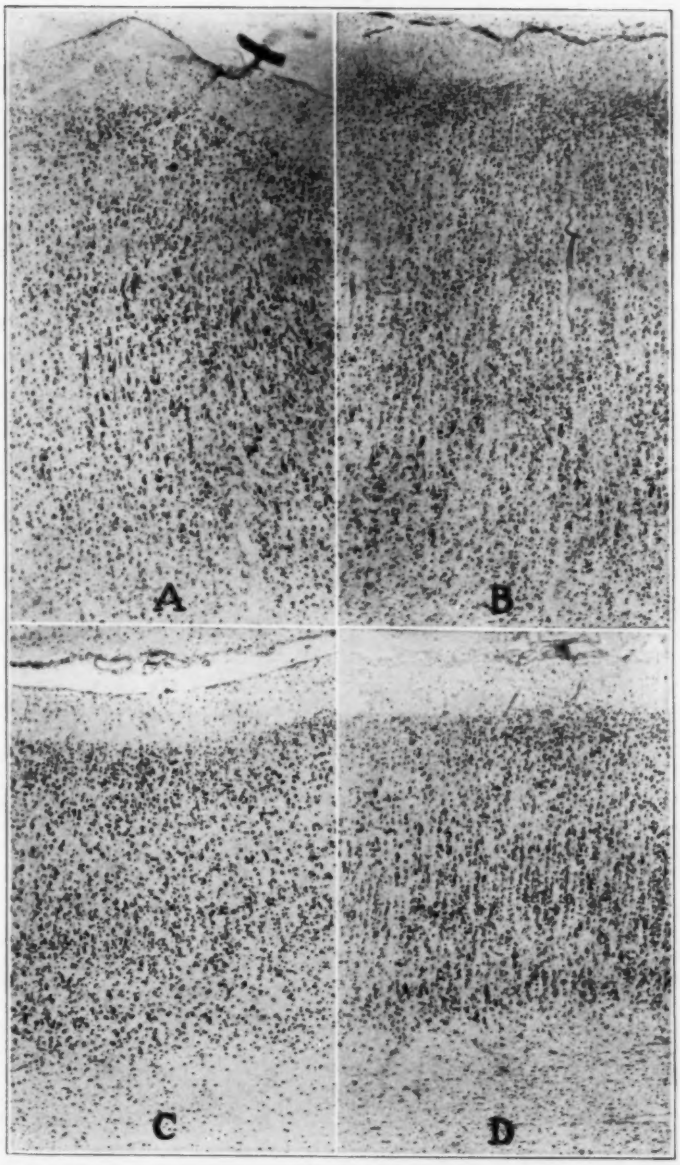

Fig. 2.—*A* (case 1), precentral convolution (× 30), nearly all layers showing poverty of cells; *B*, precentral convolution (× 30) from a normal infant of the same age as the patient in case 1; *C* (case 1), the parietal region (× 30), showing the third layer chiefly affected; *D*, parietal region (× 30) of a normal infant.

equally affected. In the frontal granular region, figure 3 *A*, the second layer as well as the third shows a marked poverty of cells. The temporal region again shows the condition confined largely to the third layer (figs. 3 *C* and *D*).

The microscopic picture of the white matter was normal except for the presence of several areas of demyelinization affecting at times only a few fibers, which

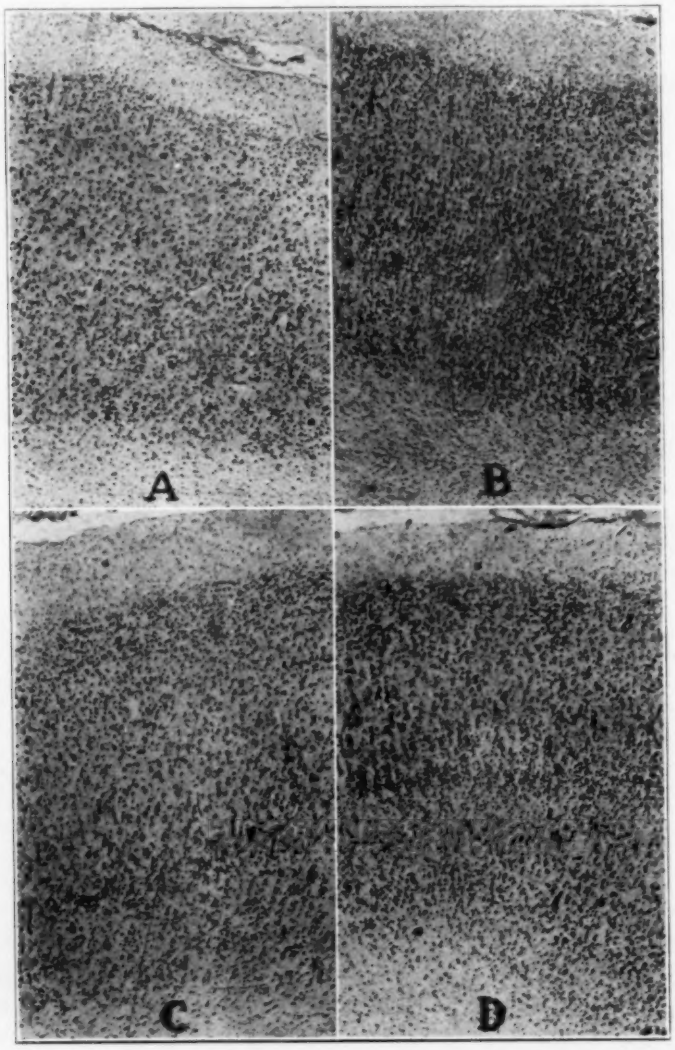

Fig. 3.—*A* (case 1), frontal granular region (× 30), showing poverty of cells in both the second and the third layers; *B*, frontal granular region (× 30) of a normal infant of the same age as the patient in case 1 shown for comparison; *C* (case 1), temporal region (× 30), showing the poverty of cells chiefly confined to the third layer; *D*, normal corresponding area from the temporal region (× 30).

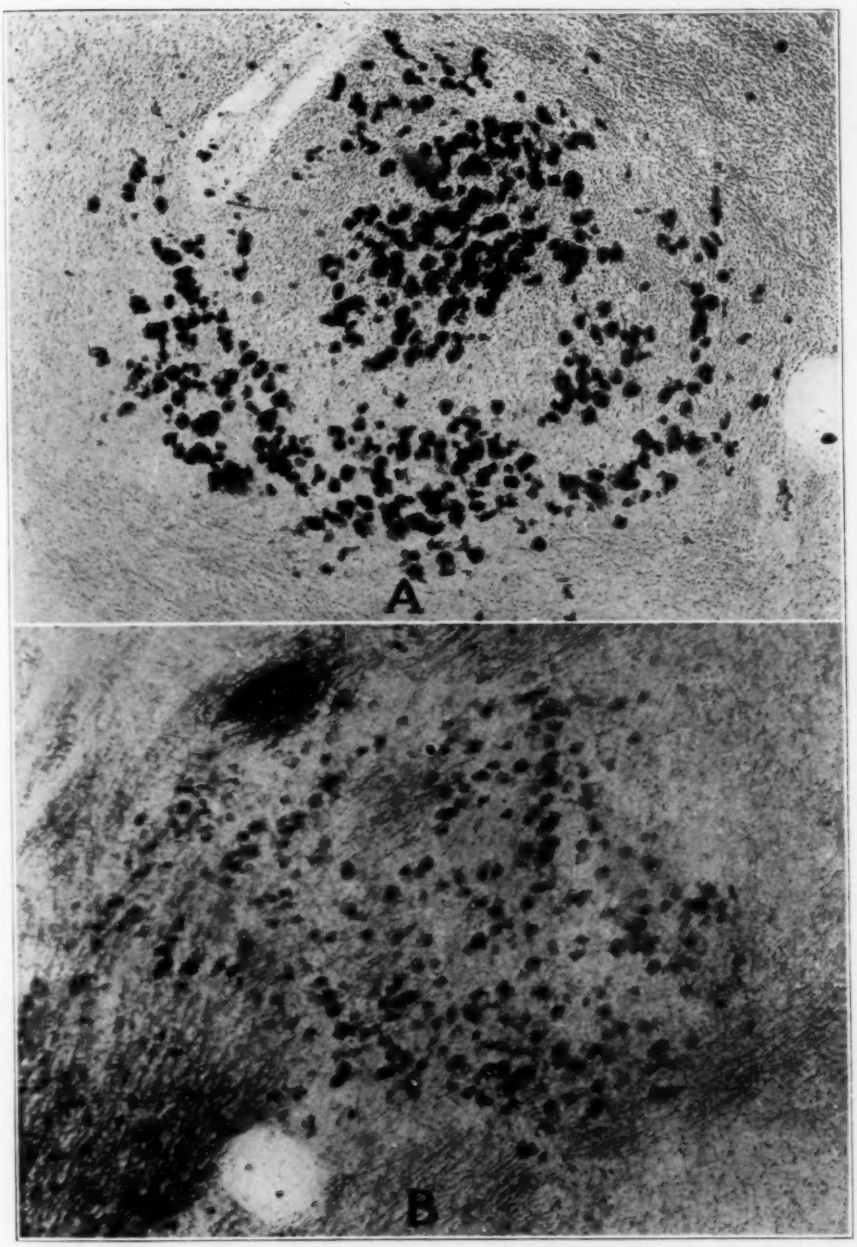

Fig. 4.—*A* (case 1), fettpenseau stain (× 115) for fat, showing an area filled with granular corpuscles; *B* (case 1), same area as in *A;* myelin sheath stain (× 115), showing granular corpuscles taking the myelin reaction.

could be followed for a considerable distance in myelin sheath preparations. Along the paths of these degenerating fibers were granular corpuscles, either singly or in groups, staining brilliant red in preparations for fat and also taking the deep blue tone of the myelin fibers (figs. 4 *A* and *B*). These areas were almost wholly confined to the neighborhood of the ventricular system. A somewhat larger collection of granular corpuscles is shown in figure 5, photographed from a toluidine blue preparation. This area seemed to differ in character from the others; the cells, in addition to vacuoles representing fat, also contained pigment which gave the iron reaction and showed a pseudocalcareous reaction in hematoxylin and eosin preparations.

In summary, this case presents clinically a typical picture of mongolian idiocy in a child, aged 11 months, who died of inanition and

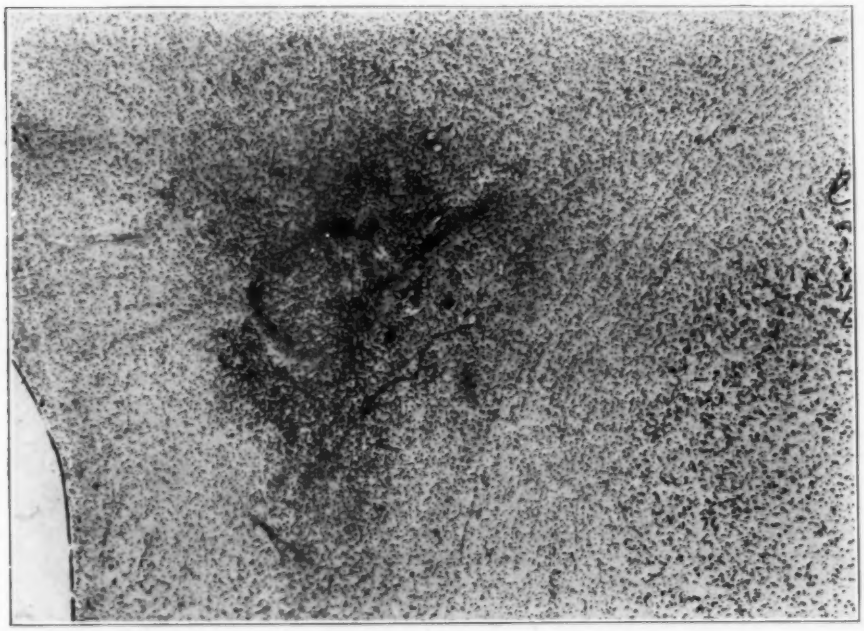

Fig. 5 (case 1).—A toluidine blue preparation (× 30) of a larger area of periventricular degeneration.

pneumonia. The brain was small as compared to the normal; the cerebellum and brain stem were relatively even smaller. Nothing was found in the microscopic examination of the latter structures to account for the diminutive size. The cerebral cortex, on the other hand, showed a distinct paucity of ganglion cells, especially in the third layer, but by no means confined to it. In the white matter were numerous small areas of demyelinization in the track of which granular corpuscles were gathered containing substances within the cell boundaries which took the stain for fat as well as a hematoxylin impregnation in myelin sheath preparations.

CASE 2.—*Mongolian idiocy; porencephaly. Relatively small cerebellum. Embryologic simplicity of cerebral convolutions; marked poverty of cells in the cortex, especially affecting the third layer. "Tuber flocculi." Absent nuclei arcuati.*

Clinical History.—K. K., an infant, aged 6 months, was brought to the hospital because of failure to develop mentally. The mother was 52 and the father 62 years at the time of his birth. He was the fruit of the eighth pregnancy and was born prematurely in the seventh month of gestation. The two preceding pregnancies resulted in miscarriages, the earlier ones in normal full-time deliveries. The living children were grown and well, except that one brother had rheumatic fever when the patient was admitted to the hospital. Following birth, the patient was unable to swallow or to cry for two weeks. He was fed with a medicine dropper and gradually began to take food. He grew physically, but failed to develop mentally.

Examination.—The boy presented a typical mongoloid facies. The head was held constantly turned toward the right; it was distinctly asymmetric with prominences anteriorly on the right and posteriorly on the left side. Practically, the only sign of life was a movement, in and out, of the tongue. The extremities were all flaccid. He failed to grasp or play. On being lifted, he could not hold up the head. An eczematous rash was present in the body folds. After a month in the hospital, following gradual daily rises in temperature without demonstrable signs of infection, he died.

Necropsy.—The lungs showed some areas of atelectasis. The gonads and suprarenals seemed too small for the age of the child. The ventricles of the heart were somewhat dilated; otherwise the organs were normal.

Brain.—The head showed the asymmetry mentioned, and the brain presented a large porencephalic defect in the left sylvian fossa, involving particularly the insular tissue and extending posteriorly to the precuneus.

The weight of the whole brain was 760 Gm.; that of the cerebellum and brain stem, 90 Gm. This makes a ratio of 1:8.4, again a distinctly small brain stem and cerebellum as compared to the relative size of the brain as a whole. The latter, in this case, in spite of the porencephaly, cannot be considered underweight for a child of 7 months.

The right hemisphere, and the part of the left one unaffected by the porus, showed the same type of wide, coarse convolutions seen in the previous case.

The meninges and blood vessels were normal.

Microscopic Examination.—The abnormalities were largely confined to the cerebral hemispheres. The nuclei arcuati, however, were represented in this brain by only two or three cells in any field. Figure 6 *A* represents the appearance of a section showing this nucleus as compared to a corresponding field from a normal child of the same age (fig. 6 *B*). It will be seen that there is an actual depression in the contour of the overlying peduncle almost as though it represented a scar formation, although gliosis was not demonstrable. The complete absence of the nucleus, especially in an infant, is possible even in a normal person, but as seen here represented by a few cells it seems to signify a distinct pathologic defect.

This was the only case in which the peculiar heterotopic structure called by Gans "tuber flocculi" was present. This occurred bilaterally. On the left side it was situated within the flocculus stem and on the right side in the white matter of the cerebellar hemisphere just inferior to the dentatum. These bodies were

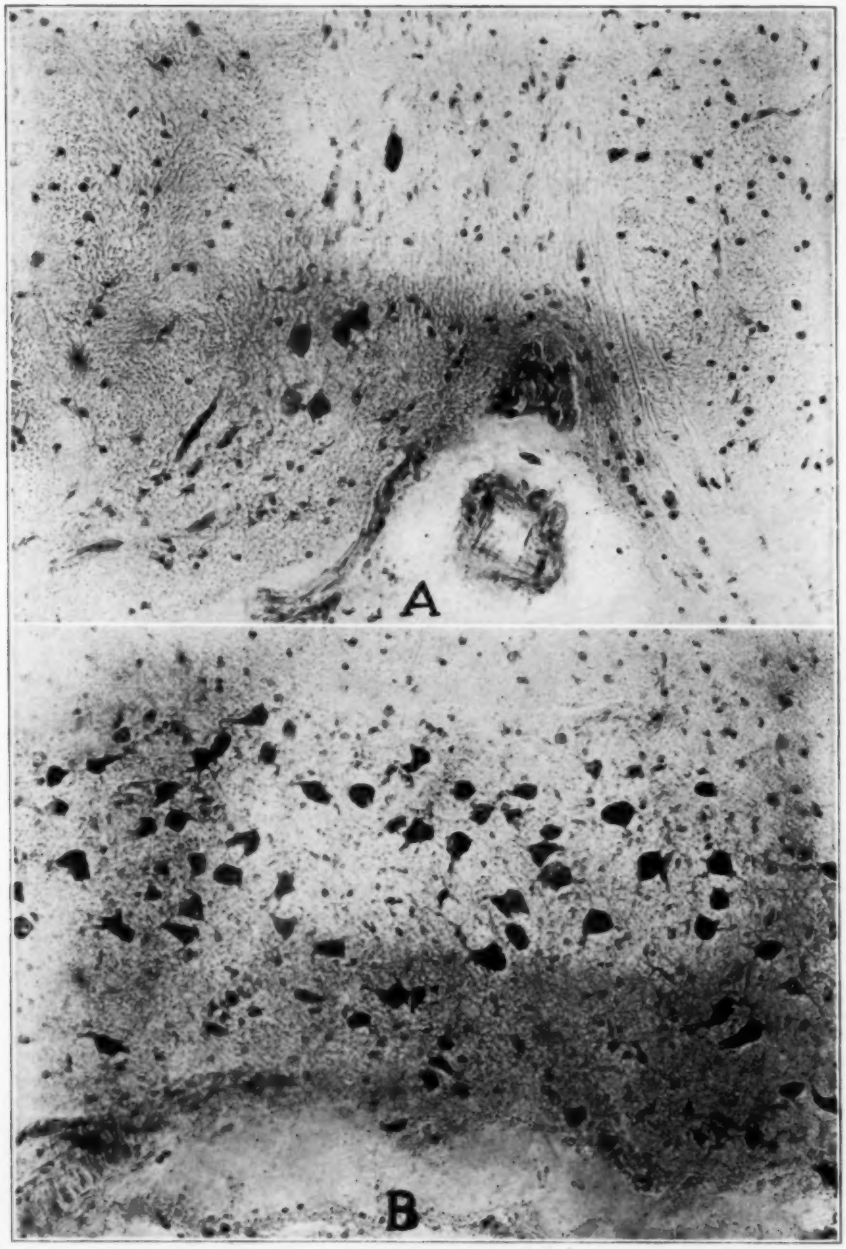

Fig. 6.—*A* (case 2), left arcuate nucleus (× 115) represented by only a few cells. The indentation is not the midline, but suggests cicatricial contraction; *B*, a normal arcuate nucleus (× 115) from same level as in *A* shown for comparison.

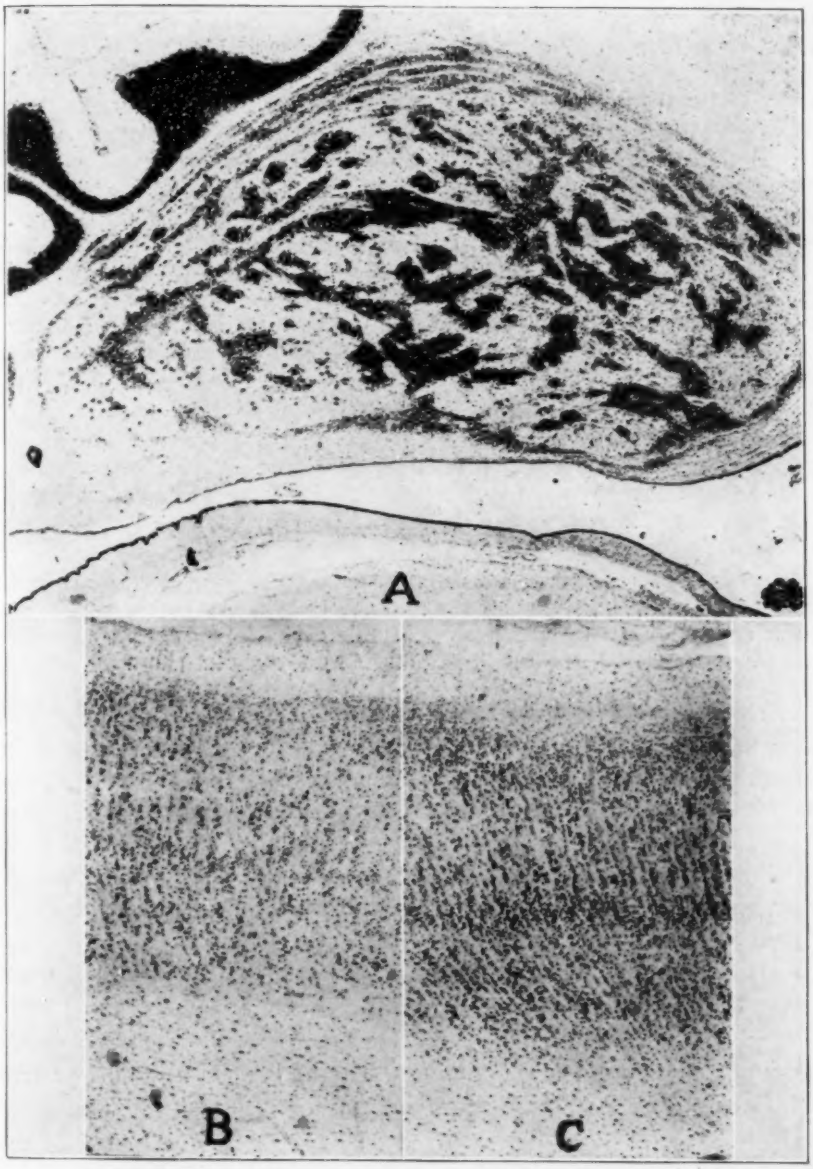

Fig. 7.—*A* (case 2), heterotopic formation in the pedicle of the flocculus (× 30); *B* (case 2), temporal region (× 30) showing poverty of cells, especially in the third layer; *C*, temporal region (× 30), showing area from normal brain to correspond to that in *B*.

oval in shape and measured 3 by 1.5 by 1 mm. and 2 by 1 by 0.75 mm. on the left and right sides, respectively. The internal structure of these anomalous formations was characterized by an absence of all architectural arrangement; the elements of which they consisted were those of the normal cerebellum—Purkinje cells, nerve fibers and cells of the granular layer. Figure 7 *A* is a low power magnification of one of these showing the chaotic state of its structure as compared with the leaflet of normal cerebellum just visible in the upper left hand corner of the photograph.

On the left side of the brain a large external porus was present and showed the usual histology of this type of lesion. The cortex was clearly demarcated from the pseudomembranous lining of the porus. Throughout the unaffected part of the cortex, the number of nerve cells, especially in the third layer, was very small. This was also true of all parts of the right hemisphere. Figure 7 *B* shows a section from the middle of the third temporal convolution, which was particularly affected. It may be seen in comparison with the corresponding area from a normal child of the same age (fig. 7 *C*) that the small number of cells is obvious practically throughout the extent of the cortical layers, although here, too, it seems to have affected the third layer particularly.

At the junction of the allocortex and isocortex in the right temporal lobe an area was found in which numerous large ganglion cells occurred in the outer granular layer and extended into the molecular layer. The character of these cells in shown in figure 8 *B*, while figure 8 *A*, a smaller magnification, demonstrates their position better and also shows the marked poverty of cells affecting all layers from the second to the sixth.

Myelin sheath preparations in this, as in the previous case, showed numerous small areas of absent myelinization. Here, also, as in case 1, the path of the absent myelin was strewn with granular cells staining deeply for fat as well as with hematoxylin in the myelin sheath preparations (fig. 9 *A* and *B*).

In this case the picture is more complicated than in case 1. The porencephaly is a new factor. Its presence, however, need not be invoked to explain any of the other changes. While granular corpuscles do result from gross destruction of brain tissue in the course of porus formation, exactly similar elements also occur in case 1 in which no porus existed. The "tuber flocculi" and the misplaced, large ganglion cells shown in figures 8 *A* and *B* are both evidence of congenital anomalies such as are to be expected in mongolism, in which anomalies are common in the heart, phalanges, teeth, bones, and other parts of the body.

The strikingly small number of nerve cells in the cortex is a factor common to both cases, as are the simplicity of the convolutional pattern and the relatively small cerebellum and pons.

Clinically, it is of interest to note that the child in case 2 is the youngest of a large family, that the parents were of advanced age at the time of his birth, and that he was preceded by two miscarriages. Van der Scheer found similar facts to apply in the greater majority of his 348 cases and believed that they lent support to his theory that

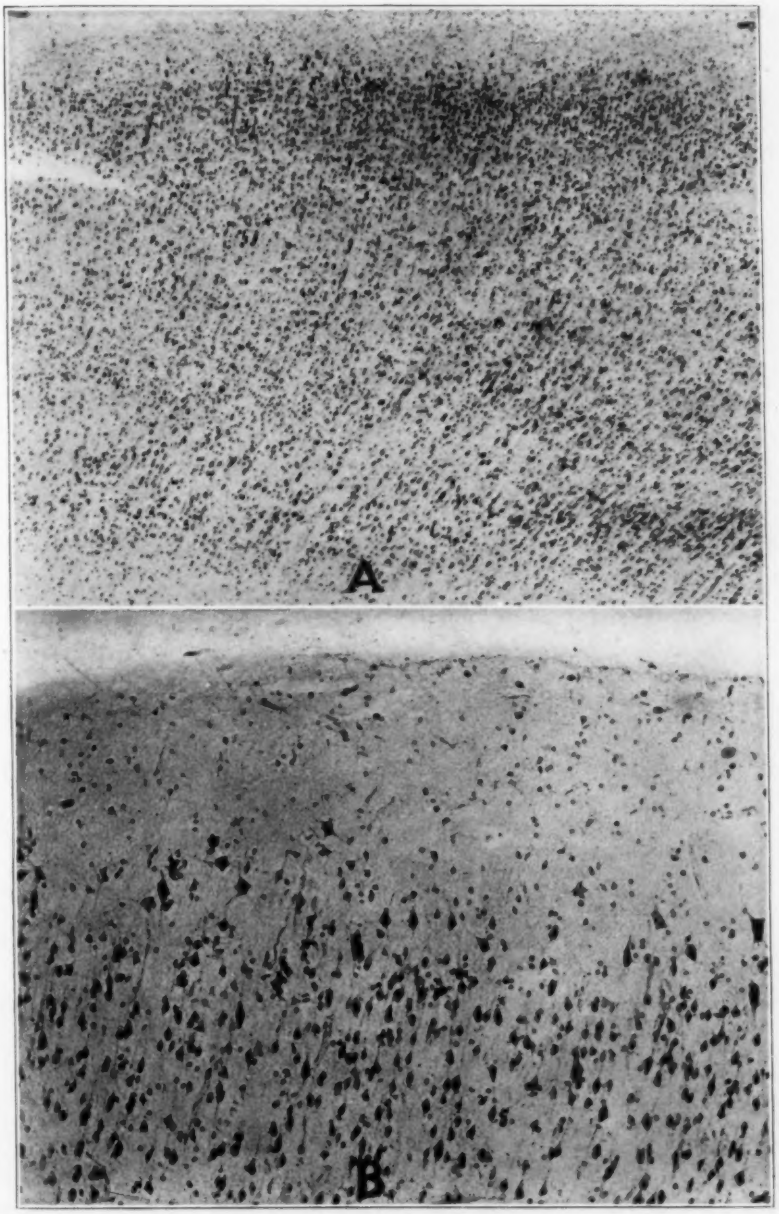

Fig. 8.—*A* (case 2), area from the border of the rhinencephalon (× 30), showing paucity of cells in all layers and abnormally located pyramidal cells in molecular layer; *B* (case 2), detail from *A* (× 115), showing the size and character of the abnormal cells.

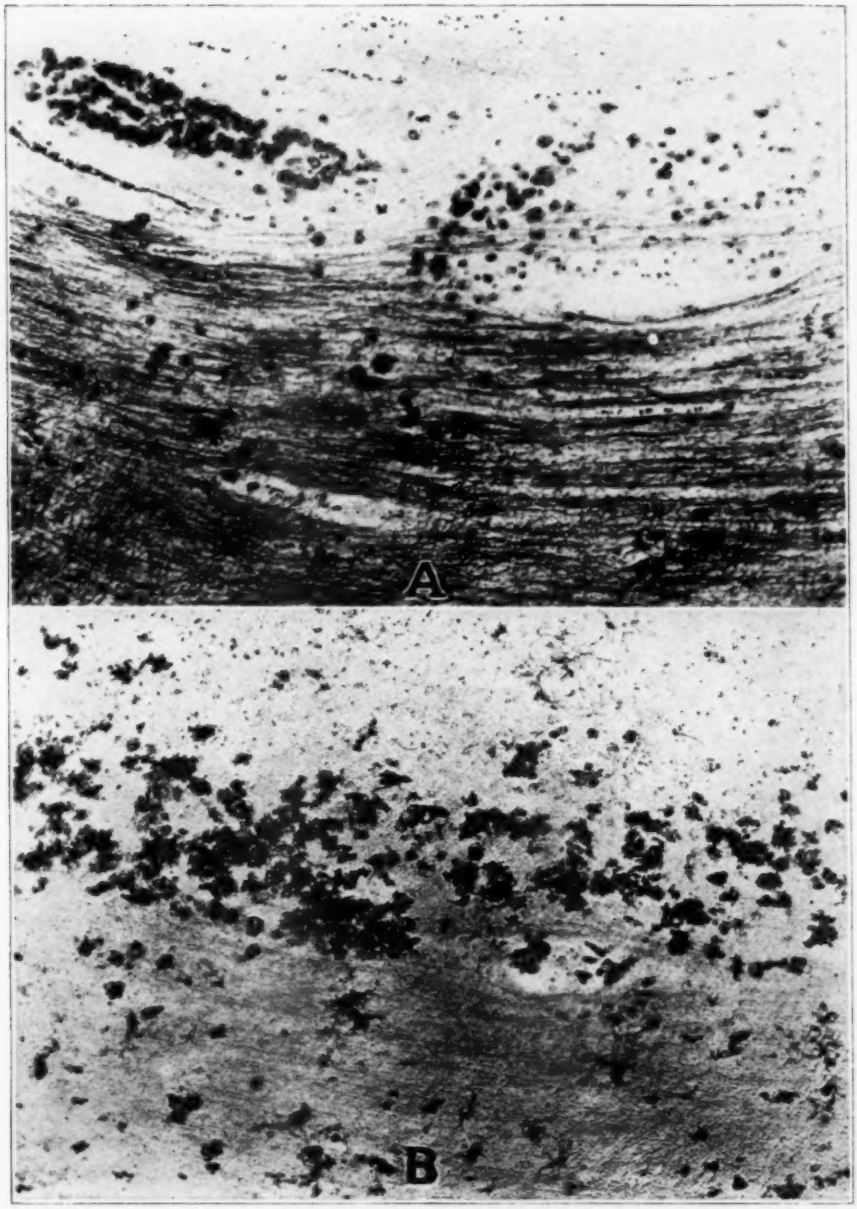

Fig. 9.—*A* (case 2), myelin sheath preparation (× 115), showing granular corpuscles taking the myelin sheath reaction; *B*, same as *A*, stained for fat.

mongolism results from too tight an amnion brought about by a pathologic uterine nidus in which the fertilized ovum was embedded in the elderly mother.

CASE 3.—*Mongolian idiot. Death from pneumonia. Normal sized brain. Small cerebellum and brain stem. Poverty of cortical nerve cells affecting especially the third layer.*

Clinical History.—H. M., a boy, aged 18 months, was brought to the hospital because of a cough and failure to take food properly. He had failed to develop both physically and mentally since birth. He was the youngest of eleven children. The parents were both past middle age. Two siblings had died in infancy but there had not been any miscarriages.

Examination.—The child presented a picture typical of a mongolian idiot, and was sick with pneumonia. The only other abnormalities found were distinctly small testes. Mentally, the child was unresponsive; he was generally undeveloped.

Fig. 10 (case 3).—The large, coarse, simple convolutions are particularly well marked in this brain; reduced one-third.

Course.—The pneumonia resolved, but the child failed to improve either physically or mentally. He remained in the hospital for three months. Toward the end of that time he began to show a daily rise in temperature, and he died suddenly of heart failure.

Necropsy.—The general observations were: bilateral pneumonia of the lower lobe; a large, soft, dilated heart, and a small fibrotic thymus. The testes were small, as was the hypophysis.

Brain.—The whole brain weighed 940 Gm., which might be taken as within normal limits for the age; but the cerebellum and brain stem weighed only 100 Gm., which is distinctly subnormal. The simple, coarse convolutions without secondary gyri are well illustrated in figure 10.

Microscopic Examination.—Abnormalities were not found in the examination of the brain stem, the basal ganglia or the cerebellum.

The cerebral cortex again showed a poverty of ganglion cells, affecting particularly the third layer but extending also into other layers. In this case the lack of cells appeared a little more focal than in the others; places could be found in which an area poor in cells adjoined a nearly normal area within the

same architectural field. This unevenness is illustrated in figure 11, taken from the parietal region and corresponding approximately to the P E field of von Economo and Koskinas.

Contrasted to case 2, the brain in case 3 showed a lack of obvious anomalies. It had in common with the others, however, the embryologic simplicity of convolutions, the distinctly small cerebellum and brain stem, and the poverty of cortical nerve cells affecting the third cortical layer in particular.

Clinically, it may again be noted that the child was the youngest in a large family and was born to parents who had passed middle age.

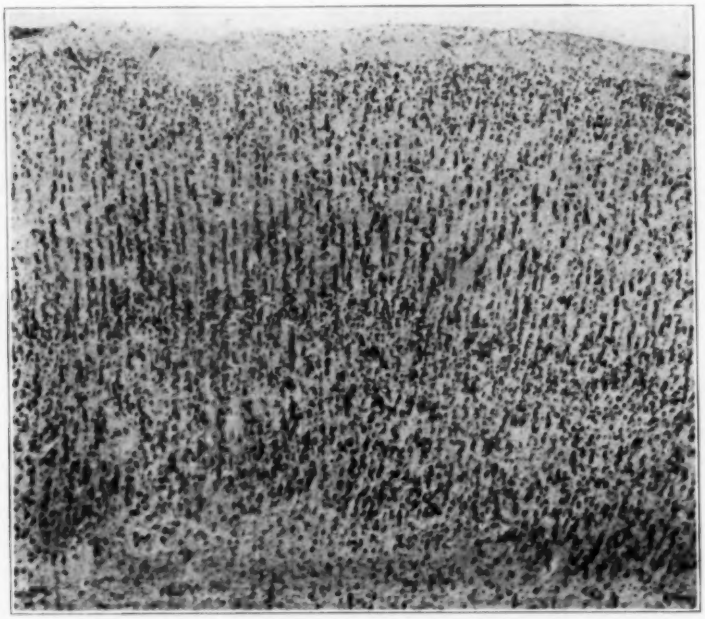

Fig. 11 (case 3).—Parietal region (× 30). The small complement of cells here is rather irregular though evident.

Case 4.—*History.*—The clinical history in this case was incomplete. It dealt with a mongolian imbecile who attained the age of 42 and died of an intercurrent infection. He was the harmless, grinning, lovable pet of the institution in which he was kept for more than twenty-five years.

Brain.—The brain as a whole and particularly the cerebellum and brain stem were distinctly smaller than normal. The convolutions were simple with few secondary gyri. The meninges and blood vessels were normal.

Microscopic Examination.—The pallidum was filled with calcium deposit (fig. 12 *A*) lying free in the tissues, especially around the blood vessels. The quantity was much greater than is found normally in this region. A considerable quantity of calcium was present also in the striatum.

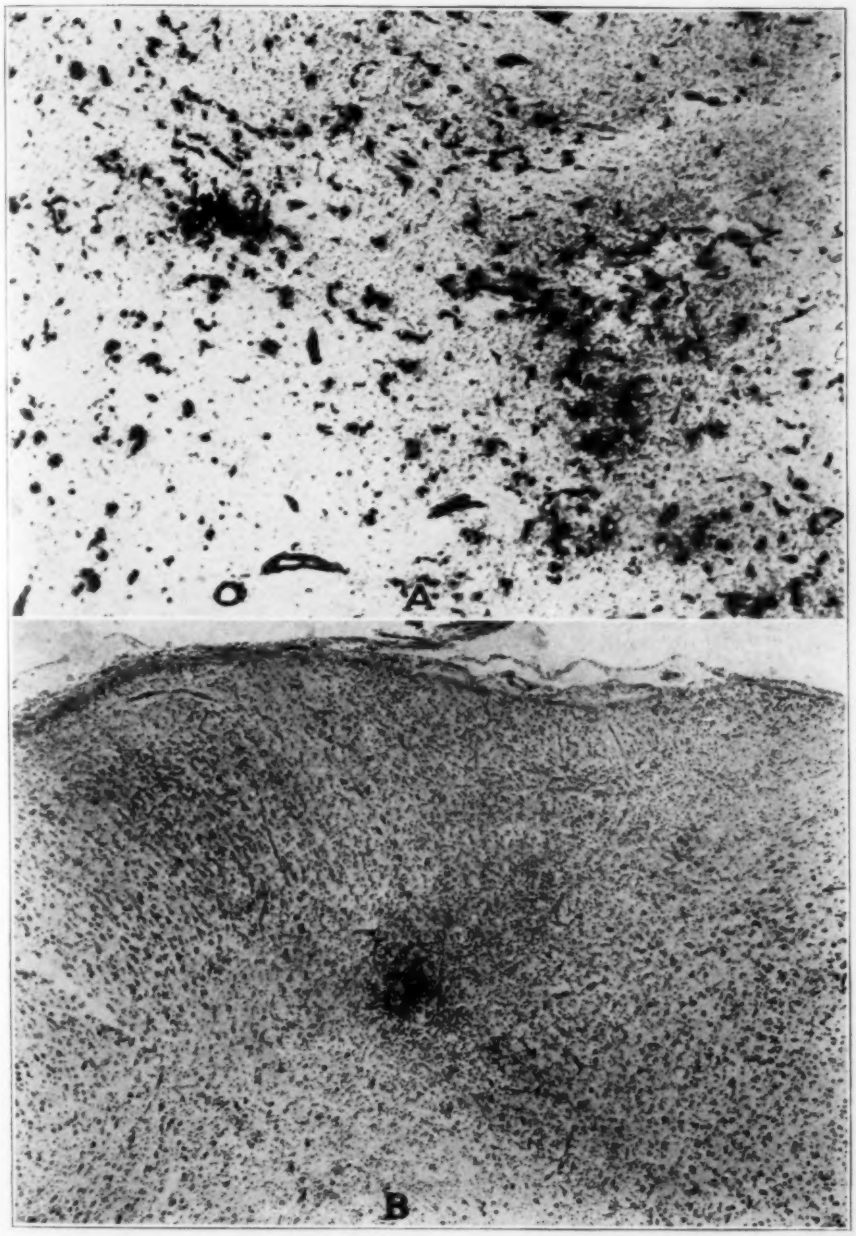

Fig. 12.—*A* (case 4), calcium deposit present in the pallidum. Stained with van Gieson's stain (× 30); *B* (case 4), ependymal-lined pocket (× 30) in the cortex.

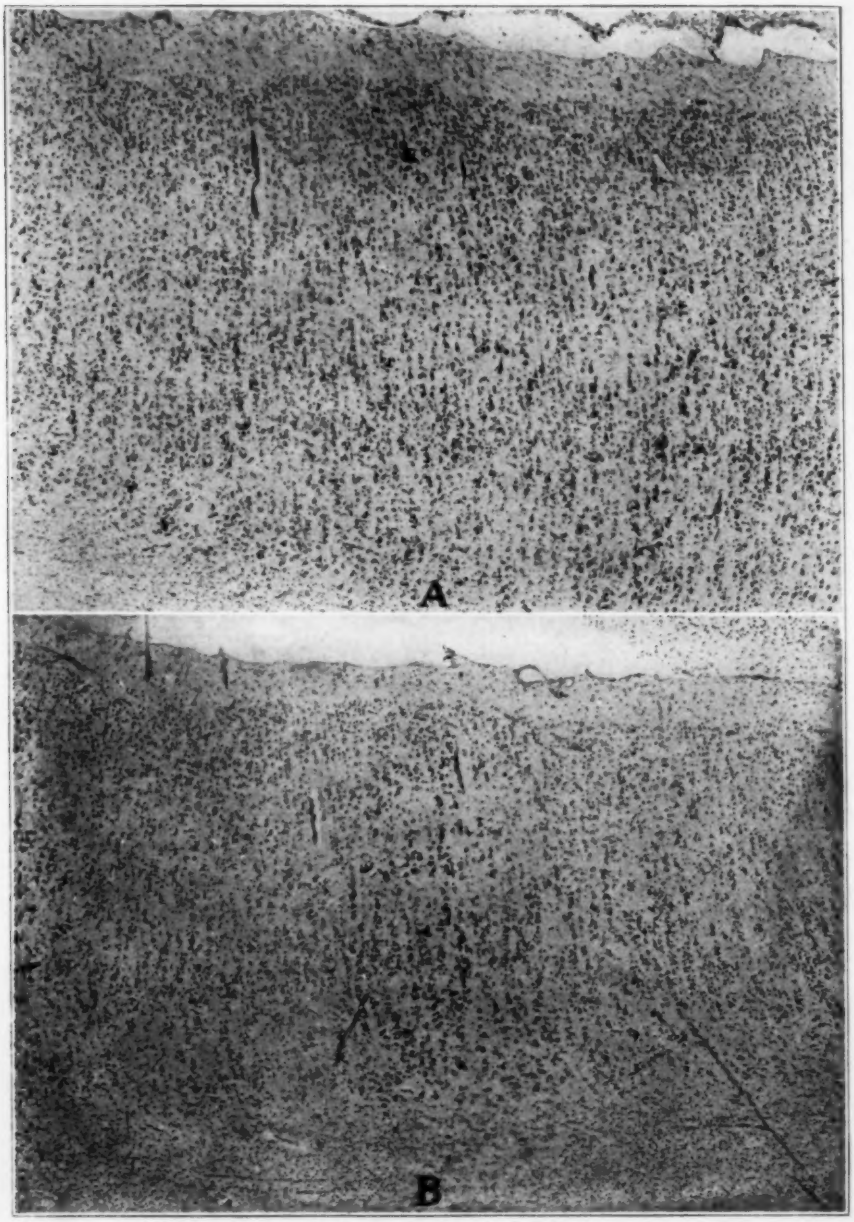

Fig. 13.—*A* (case 4), frontal granular region (× 30). The pyramidal cell content in the third layer is particularly scant; *B* (case 4), parietal region (× 30). The poverty of nerve cells is rather patchy and affects all layers, but chiefly the third.

In the parolfactory region on the medial aspect of the left frontal lobe a small area was found in the cortex where no nerve cells were present; in the center was a small ependymal-lined pocket, to which a connection could be traced with the lateral ventricle (fig. 12 *B*). Since this area was not subcortical, but distinctly within the cortex, it cannot be assumed to be merely a normal pouch of the ventricle cut at an unusual angle. It probably was a rest of the ventricular horn which extends into the rhinencephalon during embryonic life.

The general aspect of the cortex was similar to that found in the previous cases. The third layer again was chiefly affected by a poverty of ganglion cells, and, as in the others, the deficiency also extended into other layers here and there (figs. 13 *A* and *B*). Practically all areas were affected alike, although the calcarine cortex was largely spared.

Case 5.—*History.*—This was the brain of a boy, aged 10, from Hennersdorf, whose death may have been due to some infectious disease, although no history was available except that he was a mongolian idiot. It was distinctly small in size and had a small cerebellum and brain stem. This brain was particularly short and wide, with close approximation of the temporal poles. The convolutions were coarse and broad, without secondary gyri.

Microscopic Examination.—Slight infiltration of the pia and the perivascular spaces with lymphocytes may be accounted for by an intercurrent disease. There were no abnormalities in parts of the brain other than the cortex. Here the usual poverty of nerve cells was seen, again almost confined to the third layer, although other layers were also involved. Unlike the others, the polarity of the cells in this case was occasionally disturbed, although there was no evidence of cells undergoing dissolution. In spite of its small size there was no histologic evidence in the cerebellum of any abnormality.

Case 6.—This was a mongoloid child, aged 6, whose brain was sent to the laboratory from Russia. It was within the normal limits of weight, although the cerebellum and brain stem were again relatively small. The embryologic convolutional pattern was fairly well marked. Microscopic examination did not show positive pathologic changes other than that present in the cortex. Here the usual decrease in the number of ganglion cells was evident, particularly in the temporal lobes. The paucity of cells affected all layers, but was most marked in the third layer. The pia was slightly thickened, and an occasional lymphocyte was seen here.

Case 7.—This was a mongolian idiot, aged 13, from Alsterdorf. The brain resembled the others in this series grossly in its shape and simplicity of convulutional pattern. It was obviously small for a boy of 13, and had a conspicuously small cerebellum and brain stem.

Microscopically, nothing of moment was discernible except the widespread poverty of ganglion cells, largely, although not exclusively, affecting the third cortical layer.

Case 8.—This child, from Essen, was of definite mongolian type; the exact age was not recorded. Only the brain was available for study. Its shape and appearance was typically that of mongolism as judged by the shape and appearance of the other brains, although the convolutions seemed perhaps less simple in pattern than in the others.

Microscopically, aside from what may now be considered the usual poverty in ganglion cells, in this case, as in case 4, calcification was present in the basal ganglia. This was the more remarkable here since it appeared in the brain of a

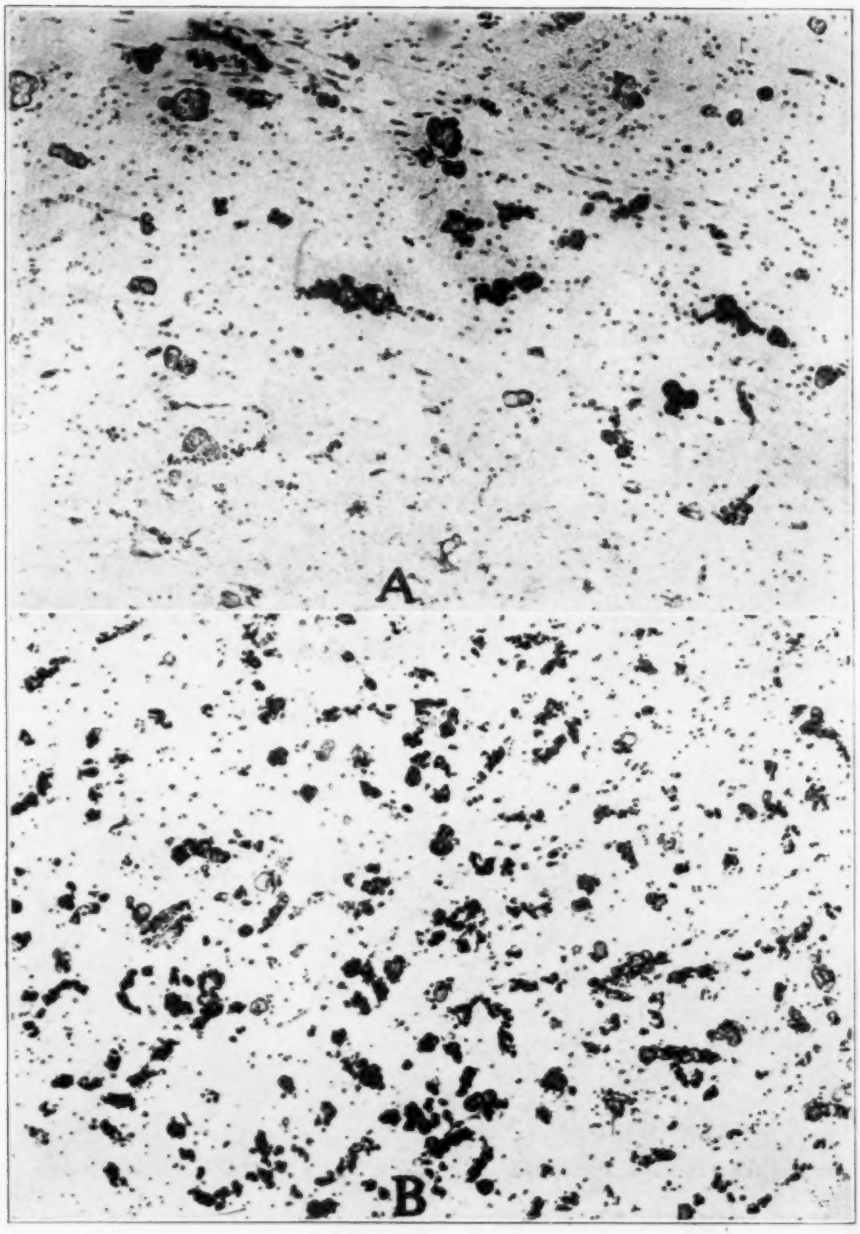

Fig. 14.—*A* (case 8), calcium deposit in the pallidum; toluidine blue stain (F 115); *B*, calcium deposit in the head of the caudate nucleus; toluidine blue stain (× 115).

child; it was also noteworthy because of the fact that the amount of calcium deposit in the head of the caudate nucleus was greater than in the pallidum (fig. 14 *A* and *B*).

CASES 9 and 10.—These two brains, sent to the laboratory from Chemnitz, had been taken from two mongolian idiot children. The ages were not stated. The gross appearance was like that of the others in the convolutional simplicity and peculiar shape. Owing to the age of the material, examination of the brains microscopically was less satisfactory than in the other cases, but the cortical changes were nevertheless demonstrable. The cerebellums and brain stems did not show any anomalies.

GENERAL DESCRIPTION OF OBSERVATIONS

In agreement with most writers on this subject, the total brain weight in my series was usually below the normal average for the age and sex of the patient. Even more constant was the disproportionately small size of the cerebellum and brain stem as compared with the brain as a whole. The relatively narrow anteroposterior and the wide lateral diameters of the brains of mongolian idiots were also noted; with van der Scheer, I assume it to be due altogether to the almost constant brachycephaly. It seems likely, moreover, that the apparent relative smallness of the interpeduncular region with the close proximity of the temporal poles to each other at the base of the brain is also due to the peculiar shape of the cranial cavity, and is not associated, as van der Scheer assumes, with an actual decrease in the size of the hypothalamic region.

In my ten cases the apparent size of the hypothalamic region varied greatly, although histologically, evidence could not be found for the assumption of either an atrophy or a failure in development of this part. In one case, in which the base of the brain resembled most closely those pictured by van der Scheer, and in which, therefore, histologic examination would be expected to disclose any abnormalities that might be present, the hypothalamic region was cut and studied in serial sections. All now known nuclei were identified. Each proved as easily demonstrable as in a normal brain used for comparison; the cells in each seemed, both in number and appearance, to be as well preserved as normal.

The description by older writers of an embryonic simplicity of convolutions with an absence of secondary gyri was confirmed to a large extent by the observations in my cases, although this varied from outspokenly large, coarse convolutions, as in case 3, to a nearly normal appearance, as in case 8.

Other external abnormalities, such as the unusual meningo-encephalitic adhesions described by Bourneville or unusual vascularization of the pia, were rare in my cases and are looked on as the result of an unassociated intercurrent disease.

In none of my cases did I find a depression in place of an excrescence from unilateral or bilateral absence of the olives as described by Gans.

The Brain Stem.—The microscopic examination was directed (following Gans) first toward the cerebellum and brain stem. The microscopic appearance of the olives was normal in all cases. The nuclei arcuati were essentially normal in most of the cases; there was one exception, case 2, in which serial section showed only an occasional group of two or three cells in this region; these cells however, were apparently normal morphologically.

No demonstrable abnormality was detected in the pontile nuclei, or the nuclei of the cranial nerves. The basal ganglia showed cells normal in number, distribution and morphology. In two cases, the striatum and pallidum were characterized by severe calcification. In one, in which the patient lived to the age of 42 years, the pallidum was much more affected than the striatum. This calcification, although it may exist normally in the pallidum, was much beyond the limits normal for the age of 42. The second example was the more striking; the patient died in childhood and the relative degree of calcification was greater in the striatum (nucleus caudatus) than in the pallidum. The calcareous material appeared greenish-blue and refractive to light with toluidine blue stain, almost black in hematoxylin-eosin preparations, and dark brown with van Gieson's stain. It replaced the parenchymatous tissue and the walls of the blood vessels in the adjacent area contained this substance; the greater amount, however, appeared to lie independent of the blood vessels, although whether it was in phagocytic cells or in ganglion cells was not determined.

The substantia nigra, in all cases examined, did not show any abnormalities. The corpora geniculata lateralia appeared histologically intact.

According to Gans, the striae Piccolomini (acusticae) were absent in four cases of adult mongolism which he examined for this structure. These striae, as known, stand in relation to the nuclei arcuati, but do not appear normally until the second year of life. All four cases showed poor development of these nuclei with absence or poor development of the striae Piccolomini. The only one of my cases in which the nuclei arcuati were poorly developed was that of a child who died at the age of 7 months; at this age the striae would not be present.

Cerebellum.—In all cases, an examination of the cerebellum microscopically showed well differentiated layers with Purkinje cells, which were normal in appearance, number and location; no double or multinucleated Purkinje cells were found. In case 2 there appeared, in an otherwise normal cerebellum, in the neighborhood of the flocculus pedicle on each side, an area consisting of a mixture of granular cells, Purkinje

cells, and molecular material, that is, normal cerebellar constituents, in irregular formation. On one side this appeared to lie within the continuation of an elongated flocculus pedicle; on the other side it occupied a more central position in the white matter of the cerebellum. Similar formations in the cerebellum have been described in four cases of mongolism by Gans who looks on it as a heterotopy. Professor Jakob believes that this structure is a failure to regress on the part of embryonic cerebellar tissue which normally exists in the region of the pedicle of the flocculus during fetal life and disappears before birth.

In one case, that of a child aged 7 months, a large external porus was found on the left side which had not been suspected clinically. This was in the usual position along the middle cerebral artery and presented histologically the usual porencephalic picture with the exception that, external to the membrane that divides the remaining cerebral tissue from the cavity of the porus, a considerable number of fat-bearing granular cells were present. This may probably be explained by the youth of the patient in that the clearing away of débris had not yet been completed.

Cerebrum.—At first glance the impression obtained from microscopic sections of the cerebrum is that of an essentially normal brain. On the whole, the pia is normal. In two cases the pia showed a moderate degree of thickening with connective tissue increase and slight infiltration of the pial vessels with lymphocytes and plasma cells. The blood vessels in these cases, as well as in all the others, were intact and showed none of the thickening described by some older authors. Closer inspection of the ganglion cells did not reveal distinct abnormalities other than those which could be accounted for by postmortem changes or by the immediate cause of death. The embryonic type of ganglion cell thought by Weigandt to be characteristic of this disease was not found in any of my cases. Bielschowsky silver preparations from various parts of the cerebral cortex as well as from the cerebellum did not show disturbances of the neurofibrils.

The glia nowhere gave an impression of being stimulated, and Victoria blue stains for glial fibers did not show an increase of the latter.

Comparison of the architectural structures of the cortex, with corresponding fields of normal brains from patients of the same age revealed that although the polarization of the cells was usually normal, their number in most cases seemed low. More careful examination demonstrated that paucity of cells, while it may affect other layers, seemed especially to have affected the third layer, practically without exception. There was never complete absence of cells, though in many places the number was extremely small. Usually, no sharply marked boundaries existed between areas poor in cells and those retaining a

normal or almost normal number of cells. The different areas, nevertheless, varied greatly in the degree to which they were affected. Although the entire cortex showed this defect, it was probably most marked in the temporal lobe. The frontal, parietal and occipital lobes were approximately equally affected, but the calcarine area often showed a better cell content than the other parts of the brain. This area, however, as already described by Gans, showed a defect in the sharp delimitation between the layers, more especially the subdivisions of the granular layer, so that the striae of Gennari were indistinct and the whole cortex appeared a little wider than normal.

The morphology of Ammon's horn formation seemed normal throughout the series. In one case, however, there appeared, at the junction of the rhinencephalon with the isocortex, an area in which the poverty of the cells was extremely marked from the second to the sixth layer. Moreover, large ganglion cells appeared scattered irregularly in the molecular layer. These were too large and too far displaced to be explained as normal elements of the cell islands or glomeruli which normally occur in this region.

In another case, a cortical area was found in the lower half of the middle aspect of the frontal lobe, within the FH field of von Economo and Koskinas, within which was an island of ependymal cells, a connection from which could be traced to the frontal horn of the lateral ventricle. This might be regarded merely as an oblique section through a normal outpocketing of the frontal horn, but the facts that its position was immediately under the molecular layer and that the remaining cortical layers surrounding it were absent makes this assumption unlikely. Since, embryologically, a ventricular pocket exists in this region within the primary rhinencephalon and later regresses, this island may justifiably be assumed to be an anomalous persistence of this ventricular pocket.

In two cases, fat preparations showed several islands of fat-filled granular cells located in the periventricular white matter. One of these cases was that of the patient who also had porencephaly, but the presence of granular corpuscles was less marked in this case than in one uncomplicated by porus. The section immediately adjacent to those taken for fat preparations, which was stained for myelin sheaths, showed an absence of myelin in the corresponding areas, and the granular cells contained protoplasmic inclusions which stained deep blue by this method, that is to say, they took the same stain as the myelin.

COMMENT

In a disease like mongolian idiocy, the sufferers from which resemble each other so closely in clinical appearance, a common pathologic pic-

ture might be expected. The morphologic changes described in the literature, however, fail to show any marked degree of unaminity.

The series of cases I have described contains a sufficient number of examples to test all the points that have been emphasized by different authors. While in particular cases their observations are largely confirmed, I have found few morphologic changes that are constant, with the exception of: a small cerebellum and brain stem, the embryonic convolutional pattern, and my own observation of the small content of ganglion cells of the third cortical layer. The process by which the latter defect arises cannot be determined with certainty from the appearance of the preparations. It might have been due either to a degenerative process now completely at an end, or to a primary failure of development. If the latter is correct, one should find no evidence of a degenerative process, past or present. This was true except in cases 1 and 2 in which myelin-bearing granular corpuscles were found. It may be of significance that these two brains were both from patients under 1 year of age. It is not unlikely, therefore, that a degenerative process affecting the ganglion cells, particularly those of the third cortical layer, occurs very early in life, and that in my youngest patients the last traces of this are still in evidence in the form of granular corpuscles filled with the remains of the myelin from the axons belonging to the degenerated cells.

However the deficiency of nerve cells comes about, the small cerebellum and brain stem, as well as the embryonic pattern of the convolutions, must be due to some factor which inhibits their growth. The difference morphologically between the cerebellum, for example, of a mongolian idiot and a normal child of the same age, seems to me comparable to that which exists between the cerebellums of normal children at two different ages. That is to say, the cerebellum of the mongolian child has failed to grow commensurately with the actual age; the same is true of the brain stem. In a modified sense this also applies to the cerebral convolutions which have been inhibited, not only in growth, but also in development so that they resemble the pattern found in early life.

One is led, therefore, to the conclusion that the brain in mongolian idiocy shows: (1) agenesis—as evidenced by cell poverty and failure of gyral development (there probably is also a degenerative process in very early life, increasing the paucity of the ganglion cells in the cerebral cortex); (2) aplasia—as shown by its small size in comparison with that of children of corresponding age, and (3) paragenesis—as demonstrated by the frequent occurrence of anomalies.

REMOVAL OF A TUMOR FROM THE SPINAL CORD IN SYRINGOMYELIA

ITS HISTOLOGY AND RELATIONSHIP WITH THE EPENDYMA *

ANDREW H. WOODS, M.D.
PEKING, CHINA

That tumors form at one or more levels of the spinal cords of patients suffering with syringomyelia is well known, though histologic studies of them have not often been published. They were considered to be gliomas, although many writers observed that, unlike ordinary gliomas, (*a*) such tumors do not infiltrate extensively so as to surround and include nerve cells and fibers, preexisting vessels and connective tissue elements; (*b*) they are part of a definite and peculiar proliferative process, of which they are but a local intensification, and (*c*) in these tumors associated with syringomyelia the ependyma and the undifferentiated cells lying near the central canal, which are closely related to ependymal cells, share in the proliferative process in a special, possibly a specific, way. Therefore, it will not be surprising if one finds that these tumors are composed of cells of the ependymal, rather than of the neuroglial, derivatives of the neuro-ectoderm.

The tumor to be described may be taken as representative of neoplasms associated with syringomyelia. Its morphology is therefore of some interest, particularly as it bears on the question of the possible identity of the cells of this tumor with those of the ependyma.

REPORT OF TUMOR

Macroscopic Appearance.—The tumor (fig. 1) was surgically [1] removed from the seventh and eighth thoracic segments of the spinal cord of a Chinese man who showed the dissociation of sensation characteristic of syringomyelia up to the fourth thoracic dermatome. In cross-section it was approximately the size of the normal thoracic spinal cord, and was 3.5 cm. long. It lay within the confines of the spinal cord, with slightly more of its mass to the left of the midline, and was separated from the pia mater by only a thin sheet of the dorsal white matter of the spinal cord, through which it showed as a dark bluish dis-

* From the Department of Neurology, Peking Union Medical College.

* Read by title at the Fifty-Third Annual Meeting of the American Neurological Association, Atlantic City, N. J., May, 1927.

1. Paraplegia, complete subarachnoid block, xanthochromia, and high protein and cell count of the spinal fluid, beginning cystitis and trophic troubles were present. The operation was a venture to forestall the usual unhappy results of that condition. It was performed successfully by Dr. Adrian S. Taylor. The patient improved and when discharged was able to stand.

coloration. At the two poles, it narrowed abruptly into rounded ends. Possibly thin rods of tissue like that of the tumor continued further along the central canal, but this could not be verified definitely at the operation.

There was no capsule, and the growth was easily separated from the surrounding white tracts. Little bleeding occurred from the walls of the cavity left by its removal.

Microscopic Appearance.[2]—The outside layer was formed by a condensation of fibrillar structure relatively poor in cells and blood vessels (fig. 2). It varied considerably in density and thickness in various parts of the tumor.

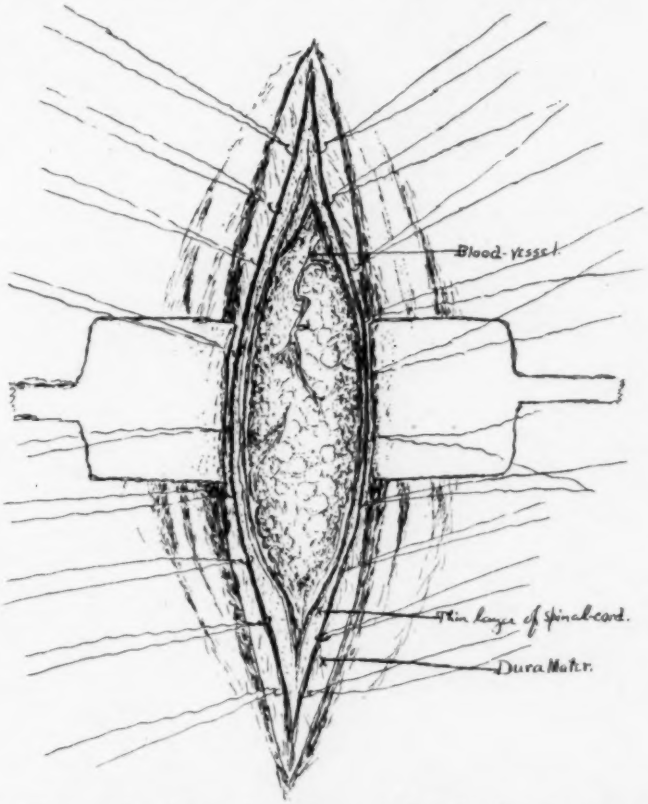

Fig. 1.—From a drawing made at the operation showing the tumor delivered through an incision between the dorsal tracts of the spinal cord.

The walls of the large and small blood vessels were much thickened and showed massive hyaline degeneration (fig. 3). The intima was often curled within the lumen. There was no proliferation of the intimal endothelium. Many perivascular hemorrhages were present, and at some points blood had dissected its way between the clusters of tumor cells and had even broken into the curbed

2. Fixation in Zenker's fluid was started within a few minutes after its removal. Sections were stained by eosin-hematoxylin, Weigert's myelin sheath, phosphotungstic acid-hematoxylin, van Gieson's and Heidenhain's iron-hematoxylin methods and by Holzer's, Achucarro's tannin-silver, and Weigert's glia-fibril stains.

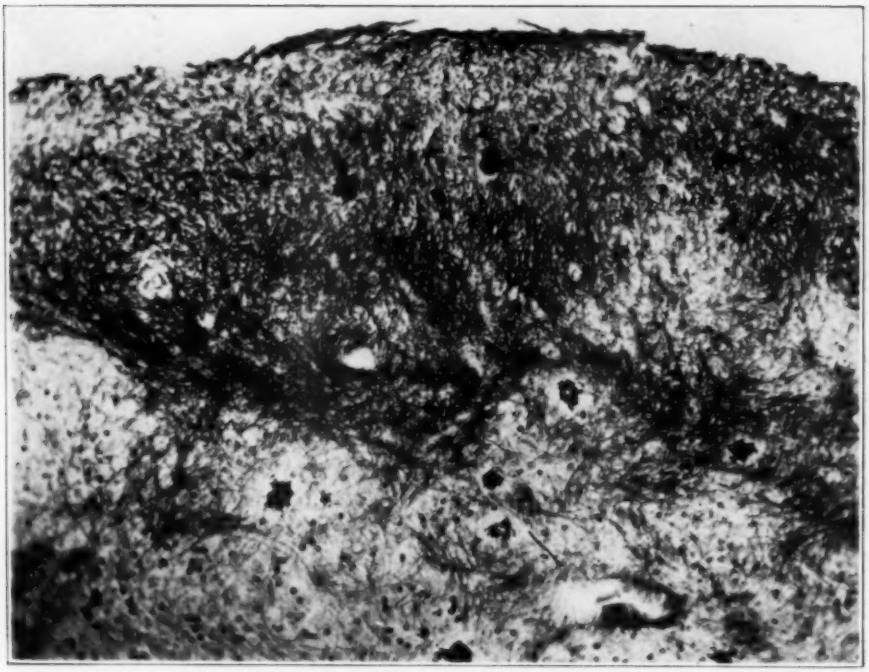

Fig. 2.—Section showing dense fibrillar network at the periphery of the tumor. Achucarro stain; × 110.

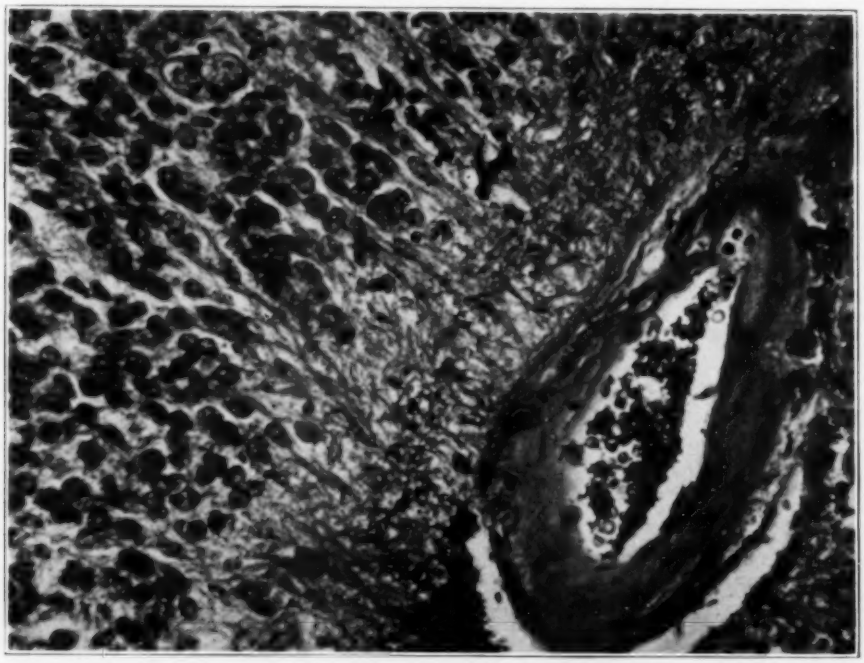

Fig. 3.—A blood vessel with thickened wall and hyaline degeneration; densely packed tumor cells, the cytoplasm of which reaches out in streamers to the vessel wall. Weigert glia stain; × 400.

cavities that will be described. Connective tissue was not found anywhere in the tumor except that in and around the blood vessel walls.

Search for remnants of the normal structure of the spinal cord failed to reveal nerve cells, axis cylinders or myelin sheaths. The new growth had not infiltrated among the structures of the spinal cord but shoved them aside.

The tumor cells had large protoplasmic bodies which in denser areas were compressed into irregularly polygonal forms. The cytoplasm of contiguous cells tended to coalesce, giving the appearance of large, polynuclear, composite masses.

Around blood vessels that were cut transversely or longitudinally, the bodies of the ordinary tumor cells were seen to narrow down in tapering cytoplasmic streamers or processes which proceeded toward the blood vessel walls. In some

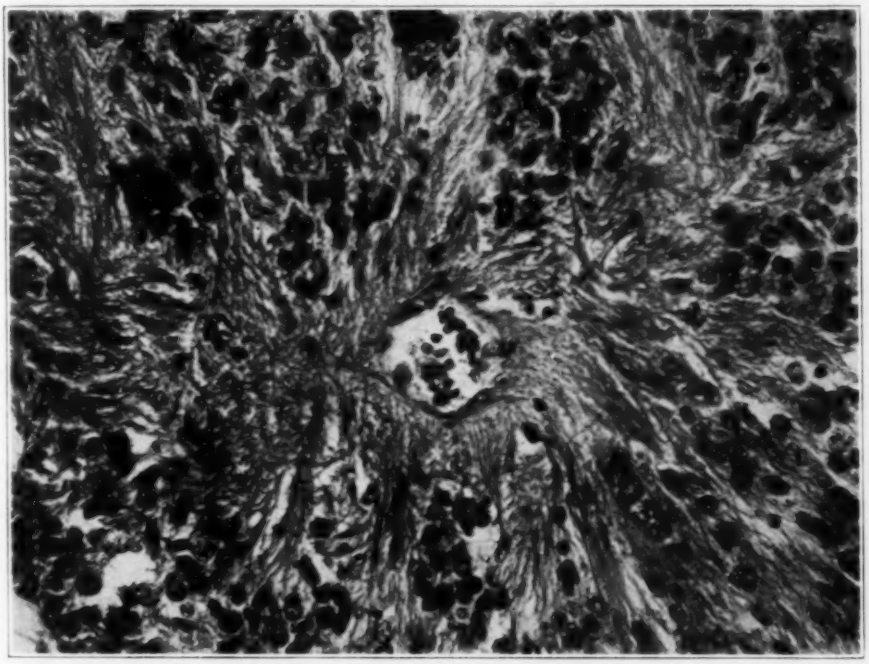

Fig. 4.—Arrangement of tumor cells around a blood vessel. Weigert glia stain; × 400.

instances, a considerable breadth of the cell body extended to the vessel (fig. 4). These extensions of the cell bodies, whether broad or narrowed into processes, did not stain deeply with the special glia-fibril stains but remained of the same tint as the general cytoplasm. With low magnification, this gave the appearance of multitudes of cell processes connecting both distant and nearby cell bodies with the vessels. The field immediately around the vessel contained few nuclei, often none, but was filled with rows of these linear elements. On both sides of longitudinally cut vessels, they lay parallel to each other; around transversely cut vessels (figs. 3 and 4) the processes converged radially toward the vessel wall.

The tumor cells, therefore, were found in clusters or rows lying at some distance from the blood vessels, and they appeared to be attached by cytoplasmic streamers to the blood vessels. The connection of a group of cells lying near a blood vessel was not necessarily with that vessel, but might be with a more

distant one. Thus the plan of arrangement throughout the tumor consisted essentially of the nutrient blood vessels with clusters of tumor cells attached to the vessel walls. No other supporting tissue was seen, except rather sparse and irregular glia fibrils.

The nuclei were large and, as a rule, oval or round, though there were many irregular forms. They varied greatly in the intensity with which they took the hematoxylin, and particularly the silver stains, some being pale, others dark. Most of them contained numbers of darkly stained chromatin granules. There were no mitotic figures.

There were also a few fiber-forming glia cells. These were entirely different in appearance from the tumor cells, being large bodied and octopus-like. They

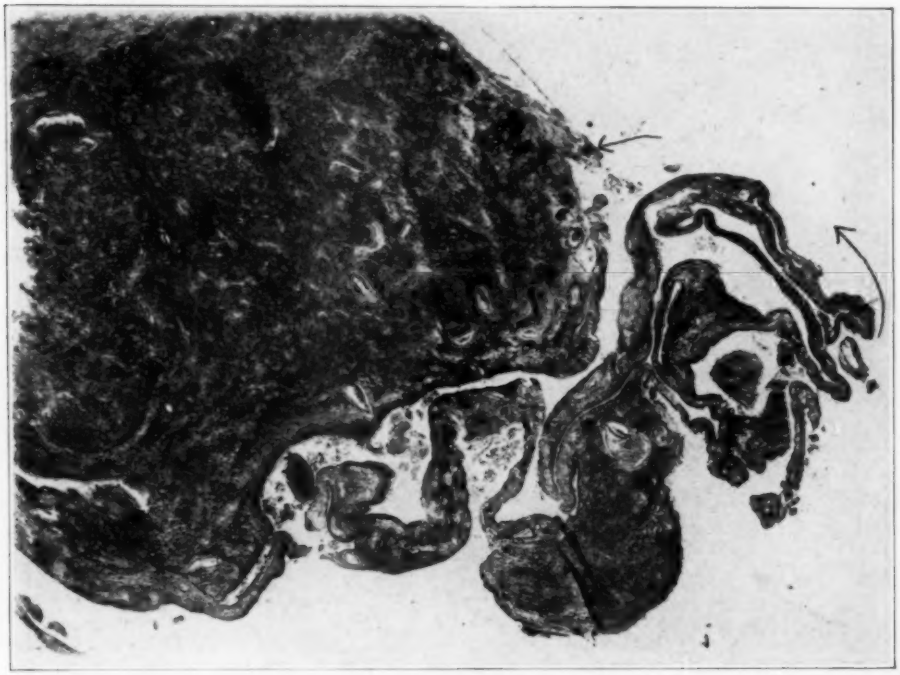

Fig. 5.—Cross-section of the tumor showing the central canal greatly dilated and tortuous, with the tumor growing from its dorsal wall. The canal wall has been torn away in sectioning. Arrows indicate points originally conjoined.

possessed nuclei which were oval and pale, and lay near the edge of the cell bodies, often looking as though they were falling out of them.

In contrast with the cytoplasmic streamers, there were distinct fibrils which stained darkly and were unevenly distributed throughout the tumor. They were well brought out by the tannin-silver and Weigert's glia stains. They were apparently of two kinds:

(*a*) The first kind consisted of long, fine, somewhat wavy and unbranched fibrils. In some fields there were only a few of these; in others, chiefly near the periphery of the tumor, they formed moderately dense, tangled mats (fig. 2). A solitary fibril was often seen to lie in or along the surface of a cell body, and thence it continued between several contiguous cells.

(*b*) There were also thicker fibrils of irregular width which were processes of the octopus-like glia cells. One or more of the processes of such a cell often could be traced to endings in a vessel wall.

The central canal was seen in all sections of the tumor as a widely dilated, collapsed tube. In cross-sections it showed complicated outlines that were produced in several ways: by the folding of its wall, by diverticula extending from the lumen often far into the tumor, and by trabeculae extending finger-like from the wall into the lumen (fig. 5). At one level a slitlike diverticulum penetrated completely through the tumor to the opposite side. The wall of the canal was lined through most of its extent with cells resembling those of the ependyma

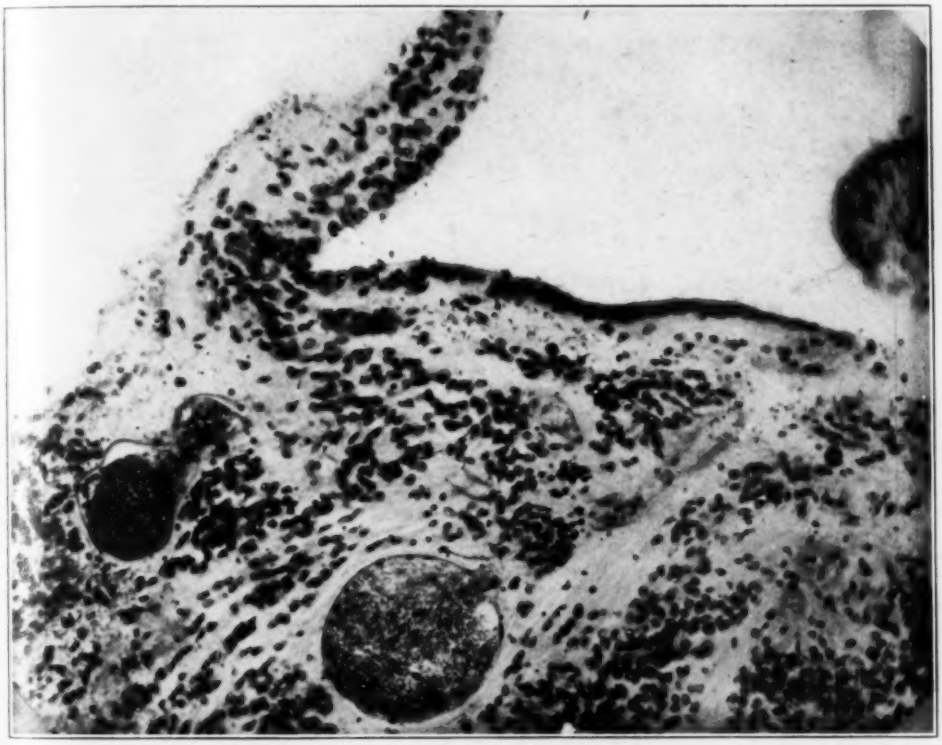

Fig. 6.—Segment of the wall of the central canal, showing a row of ordinary ependymal cells with deeply stained nuclei; other portions are without ependyma, tumor cells forming the wall. Heidenhain; × 150.

of the normal central canal (fig. 6). These cells, as a rule, lay directly on ordinary tumor cells and blended with them, but in some places a feltwork of fibrillar structure, devoid of nuclei, formed the immediate foundation. Their nuclei were like those found in the tumor cells, though inclining to oval forms with the long axes radially arranged. In some segments of the wall of the canal, the cells were imperfectly formed. At other points no ependyma was recognizable, the wall then being of fibrillar structure. The ependymal cells were in some places flattened like those of the cerebral ventricles; in other parts of the wall they were elongated in a direction perpendicular to the wall. Many had long cytoplasmic processes or strands extending among the contiguous tumor cells. If blood vessels

were near at hand, these cytoplasmic processes reached toward them. The nucleus in the elongated form of cell lay remote from the lumen of the canal. The parts of contiguous cell bodies near the lumen coalesced, so that for long stretches a continuous cytoplasmic wall was formed around the cavity. In this tumor, as in normal central canals and ventricles, the cohesion of these cytoplasmic bonds was so great that long strips or ribbons of ependyma held together when the lining was artificially broken away. On the free border of many cells, there were one or more jagged points of cell protoplasm jutting into the lumen.

Independent of the central canal, cavities were found in profusion in all parts of the tumor (fig. 7). They formed striking pictures suggesting the mouths of wells surrounded by stone curbing. Each had a central lumen around which there

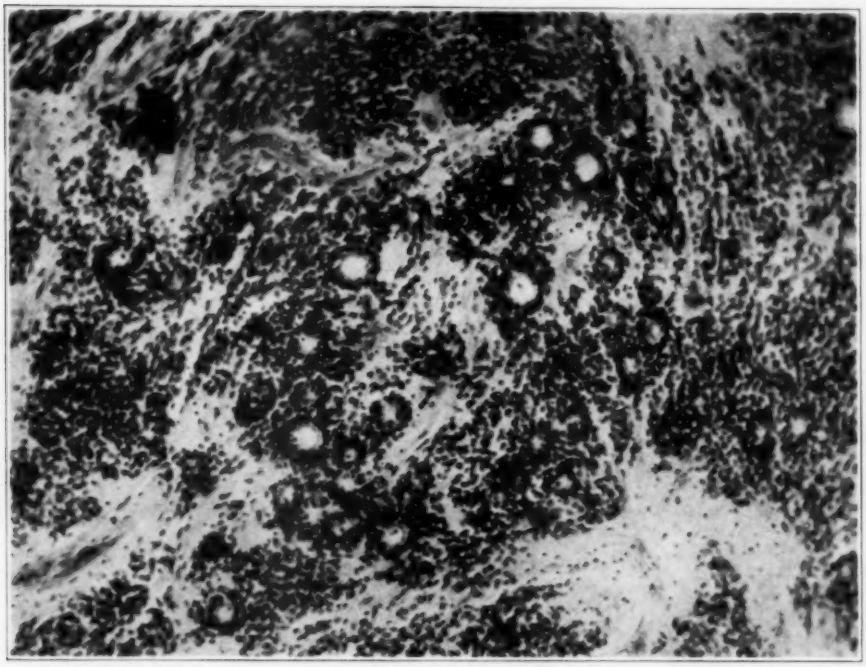

Fig. 7.—The profusion of microscopic activities, each surrounded by a curbing of ependyma-like cells. These cavities are not connected with the central canal. Heidenhain; × 100.

were one or several rows of cells with nuclei like those of the tumor cells, except that they were more often oval (fig. 8), as was observed in the cells lining the central canal. In cross-section they resembled small central canals. Serial sections, however, showed that most of them were not tubules but merely small, ovoid cavities and that they were not connected with the central canal. Their long diameters varied from 0.014 mm. to 0.3 mm. Cytoplasmic points were found here also, extending within the cavity and giving the appearance of extrusions from the cell protoplasm. No cilia could be discerned, though their absence could not definitely be affirmed because of the mingling of these cytoplasmic protrusions with the contents of the lumen. In the cells of the well defined central canal-like figures, there was a broad line across the cell body near the free edge and parallel with that edge, which resembled both in location and appear-

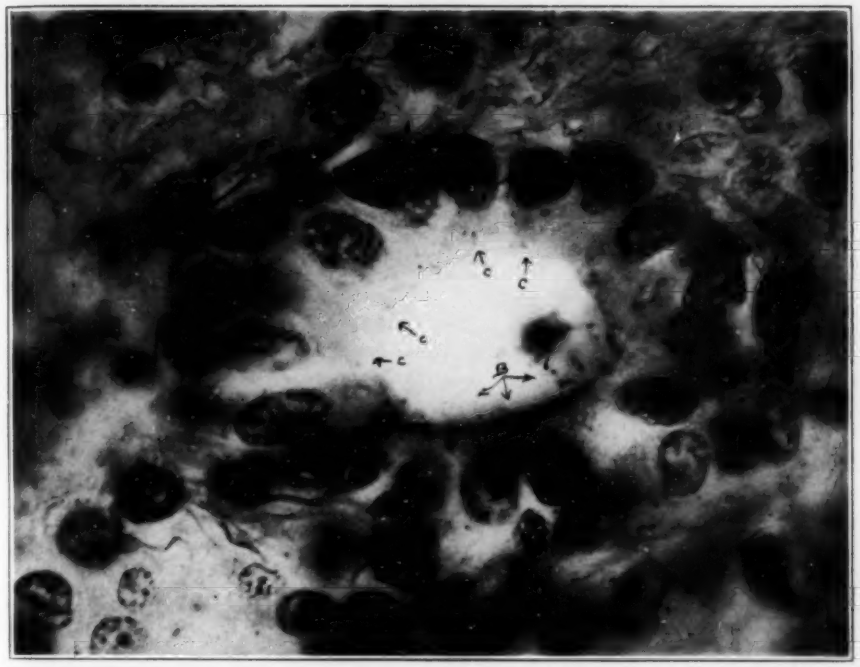

Fig. 8.—One of the curbed cavities highly magnified. Some of the nuclei of the ependyma-like cells are out of focus. *C* pairs of centrosomes in clear spaces; *B* a line of basal bodies, the remainder of the circumference formed by them being out of focus. Heidenhain; × 1,200.

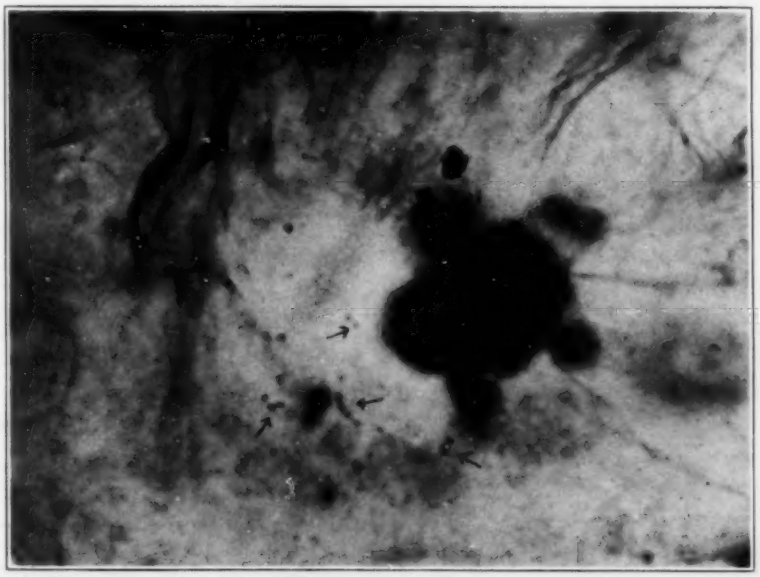

Fig. 9.—Many groups of centrosomes in the cytoplasm of ordinary tumor cells; the nuclei are not brought out by this stain. Heidenhain; × 2,000.

ance the linear marking in a cilia-bearing cell produced by the row of "basal bodies." In many instances the continuous line of basal bodies of all the cells around one cavity gave the appearance of a tunic or inner limiting membrane surrounding the cavity (fig. 8). The cavities in most cases were filled with a coagulated substance of granular appearance and containing cellular detritus. Blood elements were found in a few cavities.

The curbings were seen in various degrees of completeness, some having ependyma-like cells in only part of the circumferences, the remaining arcs being formed by ordinary tumor cells. In many places contiguous cells appeared to be just beginning to relate themselves to each other, as though about to form cavity walls. In some of these inchoate cavity walls, shadowy lines were seen in the cytoplasm near the edge of each cell body, forming more or less complete rings around the lumen, indicating that the basal body-like bands were laid down early in the process of curbing formation.

The cytoplasm of most of the tumor cells contained deeply stained granules of irregular outline. Easily distinguishable from these, however, were small dots found near the nuclei of ordinary cells, but near the free edge of the cells that lined the cavities (fig. 8). They were most distinct in the preparations stained for glia fibrils. All of them were of clear, round outline. None was rod shaped. They lay usually in pairs, sometimes apparently in threes, in small blank spaces within the cytoplasm. These dots were found most frequently in the ordinary cells (not concerned in the curbing formation) of the tumor (fig. 9).

COMMENT

The Cytoplasmic Marks.—Mallory [3] called attention to certain dots or rods which Weigert had observed in normal ependymal cells and in other cells of the same origin lying near the central canal. Mallory looked on these marks as a means of identifying ependymal cells, whether found in normal or in pathologic processes, and he described three tumors in which their presence satisfied him that the tumors were composed of ependymal cells. The words used by Weigert for these marks were merely "Körnchen" and "Punktierung," while Mallory described them as "granules," "dots" or "rods." Weigert thought that they were not parts of cilia; and neither writer attempted to identify them as any of the recognized, formed components of cell bodies acknowledged by cytologists.

Percival Bailey [4] recently discussed the general characteristics of ependymal cells, particularly with reference to the cytoplasmic markings noted by Weigert and Mallory, in connection with his valuable studies of Cushing's collection of tumors of the nervous system. In thirteen of approximately 1,000 tumors, he found certain cytoplasmic marks which he considered the same as those previously described by Weigert and Mallory; he looked on the dots found in his cases, however, as blepharo-

3. Mallory: J. M. Research **8**:1, 1902.

4. Bailey, Percival: A Study of Tumors Arising from Ependymal Cells, Arch. Neurol. & Psychiat. **11**:1 (Jan.) 1924; Some Further Cases of Ependymoma, abstr., Arch. Neurol. & Psychiat. **13**:282 (Feb.) 1925.

plasts. Most of Bailey's thirteen tumors had sprung from the region of the fourth ventricle; one was from the region of the central canal of the spinal cord. Presumably syringomyelia was not present in the case in which the spinal cord was affected, since it is not mentioned. Two of Mallory's tumors, which showed the peculiar rods or dots, were also associated with the ependyma of the fourth ventricle; one was the important tumor which he showed had been derived from embryonal rests of the coccygeal end of the neural tube. I have not found any other reports of tumors in which the subject of these markings was discussed, although Mallory's contribution was presented in 1902.

It is not satisfactory to estimate degrees of similarity between fine histologic features when one has to depend on verbal descriptions and illustrations. But the dots seen in the cells of the tumor that I have described appear to me the same as those pictured by Bailey in the communication cited; yet they are different in some characteristics from those described by Weigert and Mallory. Whether these characteristics denote that the markings in my tumor are essentially different from those of Mallory cannot be judged from data now available.

However, the double dots lying in clear spaces in the general tumor cells of my tumor are centrosomes; also, in the cells that line the curbed cavities, the paired dots lying in clear oval spaces are centrosomes,[5] and the broad band near the free margin of the cell is made up of basal bodies (blepharoplasts). The basal bodies mark the cells as potentially cilia-producing. Wilson[6] discussed the migration of the centrosome in ependymal and other ciliated cells to the free edge of the cell, and the derivation of basal bodies from it. Many centrosomes in this tumor are found in that position (fig. 9).

The centrosomes do not, of course, identify the ordinary tumor cells of this neoplasm as either ependymal or neuroglial. The basal bodies (blepharoplasts) show only that the cells containing them are cilia-bearing, which in this position means ependymal.

The Significance of the Peculiar Curbed Cavities.—The resemblance of cross-sections of the curbed cavities to cross-sections of the normal central canal is so striking that most observers have commented on it. That cells in a tumor are able accurately to reproduce a structure of such special design is of itself a reason for supposing that the cells

5. After the transmission of this report, Dr. Bailey was kind enough to examine some of the preparations. He writes that he found both centrosomes and the markings described in his report. I have not been able to discover in my preparations any rods or dots other than the centrosomes, which resemble those described by him, but hope to have an opportunity to have Dr. Bailey point them out.

6. Wilson: The Cell in Development and Heredity, New York, 1925, pp. 31 and 699.

involved in those figures are identical with those of the ependyma of the central canal. Flexner [7] was, I think, the first to suggest that these figures, seen by him in a "retinal glioma," were products of ependymal cells. He considered them efforts of the outer nuclear layer and internal limiting membrane of the retina (ependymal layer of the optic vesicle) to produce rods, cones and internal limiting membrane. Ribbert's [8] view is interesting because, while he thought these cavities corresponded to the anlages of the central canal and cerebral ventricles, he considered that certain special forms of them, seen in some of his tumors, had been derived from the germinal cells of the retina.

In this architectural tendency, therefore, there is ground for considering at least the cells that enter into the formation of the curbings as ependymal cells. Furthermore, all of the essential cells (i.e. omitting the fiber-forming glia cells) of the tumor appear to be of one type, and at any point, under some incitement unknown to us, they proceed to form themselves into these figures. This suggests that the ordinary tumor cells are identical with those that enter into the formation of the curbings of the cavities, and it gives some reason for considering all of the cells as of the ependymal cell type. The fiber-forming glia cells are mature forms. They are relatively few in number, and there is no evidence indicating whether they arose from the other tumor cells or were derived from some independent source.

Nomenclature.—The propriety of designating this tumor a spongioblastoma depends on definitions, the necessary facts corresponding to which are not yet sufficiently well established. If the essential cells of this class of tumors are proved by a reliable criterion to be ependymal cells, such tumors could be called ependymomas, or ependymal spongioblastomas, to distinguish them from spongioblastic tumors that are composed in part or entirely of neuroglia cells.

SUMMARY

The report is concerned chiefly with the description of a neoplasm which was part of the proliferative process in syringomyelia and is presumably representative of that class of tumors.

It is clear that neoplasms of this sort are not gliomas in the ordinary sense, that is tumors composed of relatively mature neuroglia cells.

The origin of the tumor from the dorsal wall of the central canal and the peculiar architectural tendencies and performances of its cells suggest that they are ependymal cells, and that the tumor is an ependymoma.

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7. Flexner: Bull. Johns Hopkins Hosp., 1891, p. 4.
8. Virchow's Arch. f. path. Anat. **225**:199 to 204, 1918.

BULBOCAPNINE IN DISEASES MANIFESTING DYSKINESIA

CLINICAL AND THERAPEUTIC OBSERVATIONS IN NINETEEN CASES DIVIDED INTO GROUPS *

JOSHUA H. LEINER, M.D.
NEW YORK
AND
M. RALPH KAUFMAN, M.D.
MONTREAL

The apparent therapeutic helplessness of physicians in adequately controlling dyskinetic symptoms in some diseases of the central nervous system justifies a trial of any drug that may give relief. Bulbocapnine has given some results of therapeutic value in the hands of De Jong and Schaltenbrand,[1] Lewy [2] and others. A study of the drug was undertaken at the Montefiore Hospital.

We selected nineteen cases presenting various dyskinetic phenomena and divided them into two groups, the first consisting of eight cases showing the parkinsonian syndrome, four of the idiopathic type and four due to epidemic encephalitis, and the second group including seven cases of multiple sclerosis, one case of Huntington's chorea and two cases of dystonia musculorum deformans. One of the latter presented a combination of abnormal movements.

The drug was administered hypodermically, the dosage being from 0.1 to 0.2 Gm. Sterile water administered subcutaneously was used as a control. The tremors in the patients exhibiting the parkinsonian syndrome were recorded on a kymograph, the index finger of the left or right hand being used. In one case the tremor of the jaw was recorded, while in the cases of multiple sclerosis, specimens of the patients' handwriting were utilized whenever possible. In three of the patients having multiple sclerosis the condition was so far advanced that they were unable to write; hence, the finger-to-finger and finger-to-nose tests were used for observing any changes in the tremor.

In the patient with Huntington's chorea and in those with dystonia, clinical observations of the changes in the movements were made. Records were also taken of the pulse and respiration rates and of the

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* From the Neurological Division, Montefiore Hospital, New York.

1. De Jong, H., and Schaltenbrand, G. S.: Die Wirkung des Bulbocapnin auf Paralysis Agitans und andere Tremorkranke, Klin. Wchnschr. **3**:2045, 1924.

2. Lewy, F. H.: Erfahrungen über die Wirkung von Bulbocapnin auf das Zittern, Deutsche med. Wchnschr. **52**:351, 1926.

pupillary response and general condition of the patients following the administration of the drug.

REPORT OF CASES

CASE 1.—*Examination.*—H. B., a woman, aged 66, had had Parkinson's disease, of the idiopathic type, for nine years. When studied she was chair-ridden. The pupils reacted to light and in accommodation; tremors were present in the hands, feet and jaws; there was marked increase of tone in all the extremities. Mentally she was alert. The respiration rate was 20, the pulse rate, 78.

Therapy.—The tremor was recorded from the right index finger. One minute after the administration of 0.1 Gm. of bulbocapnine, a slight decrease in the

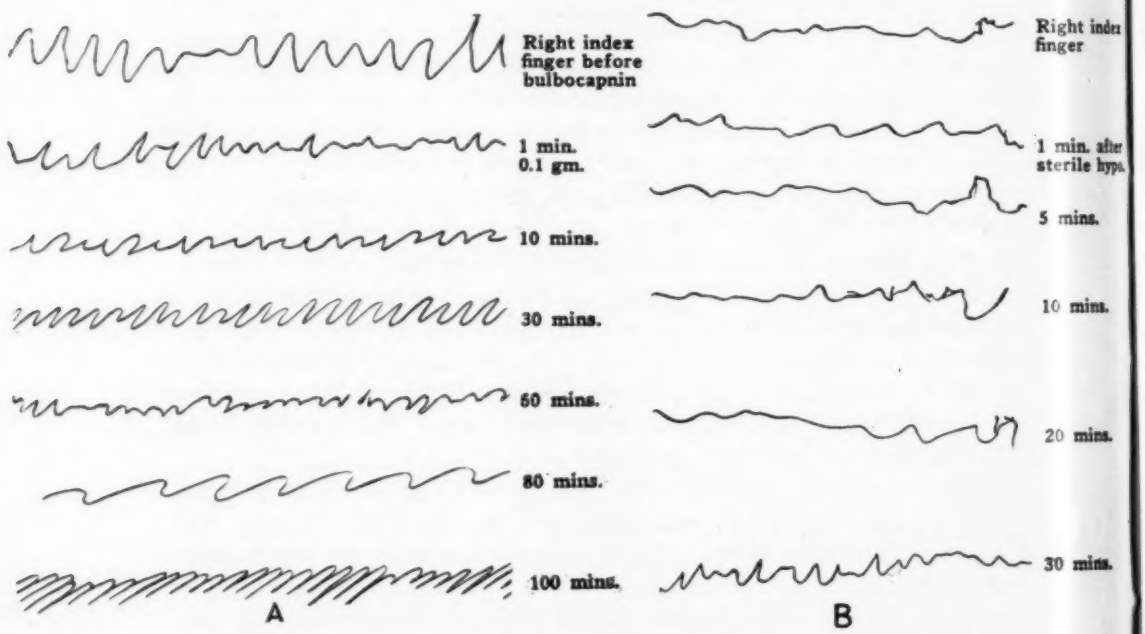

Fig. 1.—Case of Parkinson's disease, idiopathic type. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine; *B*, handwriting after administration of sterile water.

amplitude of the tremor was noted (fig. 1 *A*). This lasted for about sixty minutes and then increased gradually until at 100 minutes it was at its previous amplitude. At this time an increase was also noted in the number of tremors per second. The pulse showed slight variation, the rate being between 76 and 80. The respiratory rate varied between 18 and 22. The pupils during this time reacted promptly to light and in accommodation. There was little effect on the tremors. The patient was not sleepy. She did, however, complain of dizziness and slight headache. Tonus was not affected.

On the following day, a control record was taken after 1 cc. of sterile water had been injected subcutaneously (fig. 1 *B*). It is noteworthy that the amplitude at this recording was considerably less than on the previous day.

CASE 2.—*Examination.*—A. Y., a woman, aged 64, had had Parkinson's disease of the idiopathic type for five years. She had a pulse rate of 86 and a respiratory rate of 18.

There was a typical parkinsonian syndrome with tremors of the jaw, fingers and toes; increased tone was present in all extremities with cogwheel phenomena. The pupils reacted promptly to light and in accommodation. The patient was mentally alert.

Therapy.—One tenth gram of bulbocapnine was administered. Within one minute, the tremor in all the extremities had disappeared. This lasted for fifteen

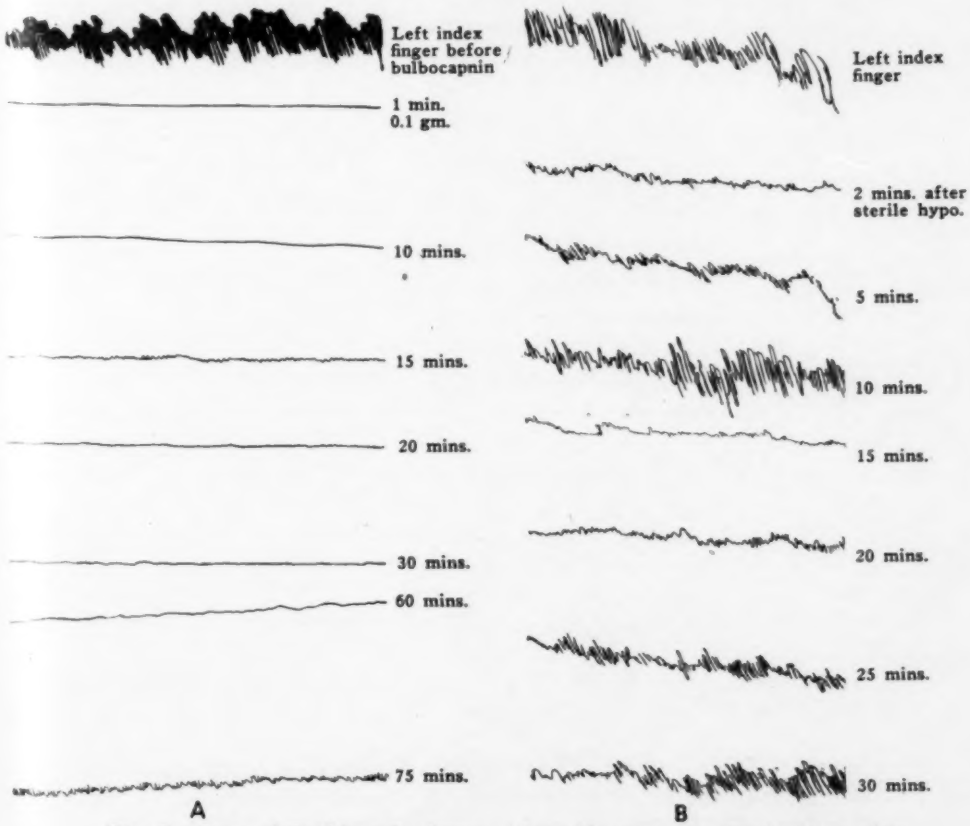

Fig. 2.—Case of Parkinson's disease, idiopathic type. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine; *B*, handwriting after administration of sterile water.

minutes, after which a fine rhythmic tremor was noted. This persisted until seventy-five minutes after the injection when the amplitude of the tremor was again slightly increased (fig. 2*A*). The pupils reacted to light and in convergence. The pulse rate varied between 86 and 88, the respirations between 18 and 22. The tonus was not affected. Clinically, there was a distinct improvement in the tremors. The patient showed toxic symptoms, was extremely drowsy and dull and complained of headache and dizziness. She was nauseated but did not vomit. She was put to bed because of these unpleasant manifestations.

In the control experiment, two minutes after the administration of the water the tremor showed a decrease in amplitude; at five minutes, however, it was slightly increased and at ten minutes had returned to its full height. It was noted that there was a further decrease in the amplitude at fifteen and twenty minutes, which increased again at twenty-five and thirty minutes (fig. 2*B*).

CASE 3.—*Examination.*—L. S., a man, aged 55, had Parkinson's disease of the idiopathic type, the tremor having been of two years' duration. General physical examination showed a glaucoma of the right eye; otherwise no abnormality was present. Neurologic examination showed a masked facies. The left pupil reacted to light and in accommodation. Perioral tremor and tremor of the fingers, toes and jaw were present. Cogwheel phenomena with hypertonicity and sialorrhea were noticed.

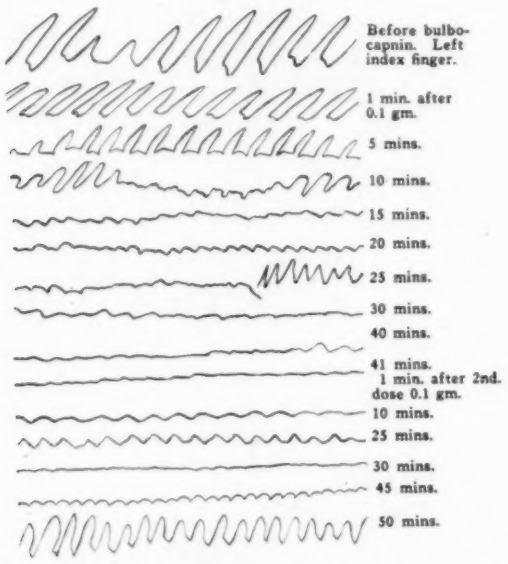

Fig. 3.—Case of Parkinson's disease, idiopathic type. Handwriting after administration of 0.1 Gm. of bulbocapnine.

Therapy.—The record was taken from the left index finger. One minute after 0.1 Gm. of bulbocapnine was administered, a progressive diminution of the amplitude of the tremor was observed, so that at forty minutes it was only slightly noticeable. Another dose of 0.1 Gm. was given and ten minutes after this a slight rhythmic tremor was noticed which gradually increased. However, at thirty minutes after the second dose the tremor had practically ceased, and a straight line was recorded on the kymograph. At forty-five minutes the tremor was again noticeable, and at fifty minutes it returned to its former intensity and was somewhat more frequent (fig. 3). Clinically, the effects on the patient were marked. The maximum diminution of the tremor was noted between fifteen and forty minutes after the first dose. The patient became dull and complained of dizziness and headache. The left pupil was moderately dilated and reacted sluggishly to light for the first sixty-five minutes after the drug was administered, reacting promptly after this time. The pulse rate varied between 90 and 96, the respiratory rate

between 20 and 22. Sterile water administered hypodermically did not cause appreciable results. A control record was not made.

Case 4.—*Examination.*—H. P., a man, aged 20, had had a postencephalitic parkinsonian syndrome since 1919; the tremor was of three years' duration. Neurologic examination showed a masked facies. The pupils were unequal, reacted sluggishly to light, and there was no reaction in accommodation. Failure of con-

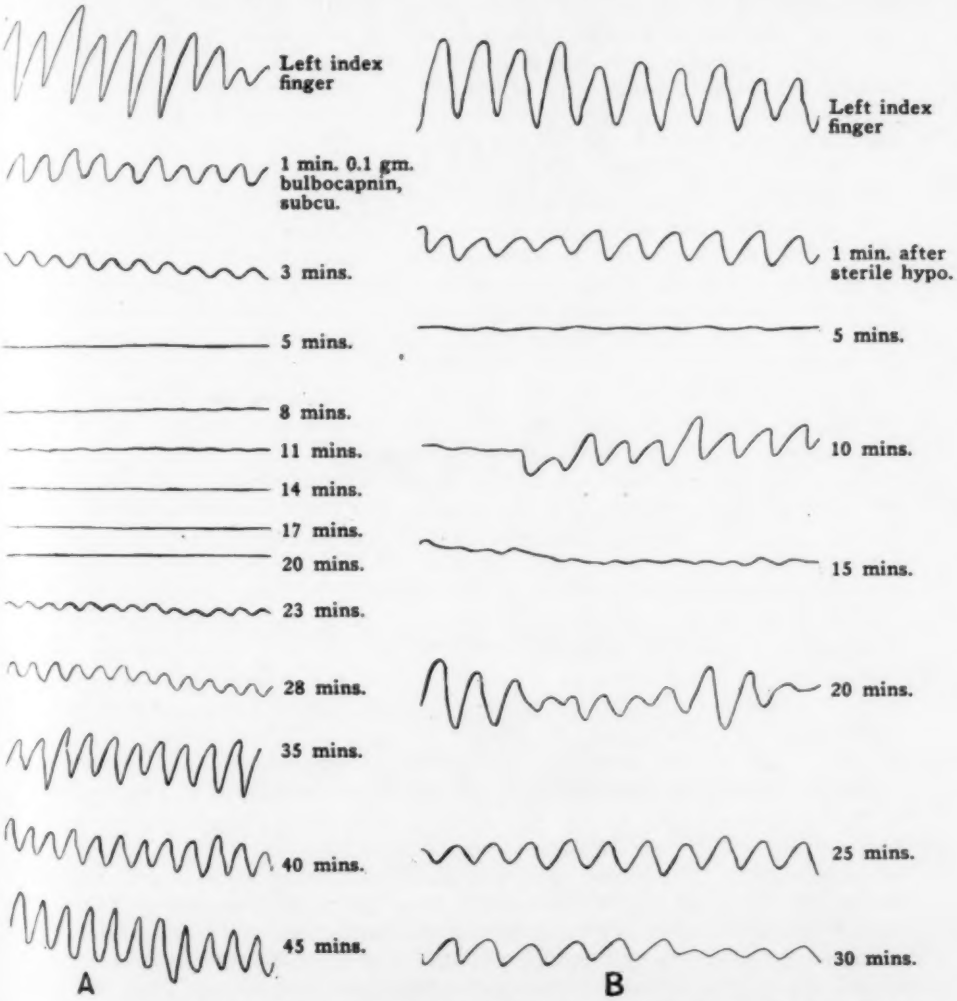

Fig. 4.—Case of postencephalitic parkinsonism. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine. *B*, handwriting after administration of sterile water.

vergence, with diplopia at 2 feet was present. There was marked tremor of the jaw, tongue, hands and lower extremities. A mild degree of hypertonicity was present. The patient was mentally alert.

Therapy.—The record of the tremor in the left index finger showed a distinct diminution in amplitude, one minute after 0.1 Gm. was given (fig. 4 *A*). At three

minutes, this diminution was still more marked and at five minutes the tremor ceased, a straight line being recorded on the kymograph. This effect obtained until twenty minutes after the injection. Records were taken at eight, eleven, fourteen, seventeen and twenty minutes. During this interval the movements of the jaw, tongue, hands and lower extremities had ceased. The patient was drowsy; the pupils, previously noted as being sluggish, were now dilated and fixed to light and in accommodation. After twenty-three minutes the tremor began to appear, gradually increasing in intensity, and reached almost its full amplitude at thirty-five minutes. The pulse rate varied between 84 and 90, the respiratory rate between 20 and 22. Clinically, there was a distinct improvement in tremor. The somnolence was marked; the patient was mentally dull and complained of headache, dizziness and nausea. At the termination of the experiment, the patient was assisted to bed and slept for several hours.

The control record showed two periods of subsidence of the tremor at five and fifteen minutes, interspersed with tremors of full amplitude (fig. 4 *B*).

Case 5.—*Examination.*—J. H., a man, aged 47, had a postencephalitic parkinsonian syndrome, the tremors having been of seven years' duration. Neurologic examination showed that the pupils reacted sluggishly to light, the left more than the right; the reaction in accommodation was normal. There was a masked facies. The tremors were irregular in amplitude and rhythm, as recorded from the left index finger.

Therapy.—After the administration of 0.1 Gm. of bulbocapnine, there was a gradual diminution in the amplitude; the rhythm became more regular, and at forty minutes only a fine rhythmic tremor was present. The duration of this period of decrease was short and at fifty minutes it again increased, full amplitude being attained at the end of eighty minutes. The rhythm, however, remained regular (fig. 5). Clinically, there was little improvement, although graphically some was demonstrable. The patient complained of headache and drowsiness; the pupils were moderately dilated and reacted sluggishly to light. The pulse and respiration did not show any appreciable change. The control experiment did not show any effects beyond the apparently normal variation.

Case 6.—*Examination.*—S. P., a woman, aged 49, had a postencephalitic parkinsonian syndrome. The general physical condition was one of undernutrition, though otherwise it was normal. Neurologic examination showed a masked facies, irregular pupils reacting sluggishly to light and in accommodation, and tremors of the jaw, hands and lower extremities. Hypertonicity was fairly well marked.

Therapy.—The tremor of the jaw was registered in this case. After the administration of 0.1 Gm. of bulbocapnine, a continuous record was taken for seventeen minutes. The tremor showed a gradual diminution at the end of one minute and almost complete cessation which lasted for twenty-five minutes. During this time the soporific effect was marked; the patient was dull, and the pupils were dilated and did not react to light. At the end of thirty-five minutes she complained of severe headache and dizziness, with nausea but no vomiting. There was a gradual return of the tremor, and at sixty minutes it had attained its full intensity (fig. 6 *A*). The respirations decreased slightly from 22 to 18; the pulse rate varied between 80 and 84.

The control record taken several days later showed an irregular tremor of the jaw with some diminution of intensity at eight, eleven and fifteen minutes (fig. 6 *B*).

Case 7.—*Examination.*—H. B., a man, aged 19, had a postencephalitic parkinsonian syndrome with tremors of two years' duration. The pupils were slightly

irregular, but reacted to light and in accommodation. A mild rhythmic tremor of the left arm and right leg was present.

Therapy.—The tracing, taken from the left index finger, showed practically no effect one minute after the administration of 0.1 Gm. of bulbocapnine. At five minutes, however, the tremor ceased, and this effect lasted for approximately 150 minutes (fig. 7). Clinically, the effect was well marked. The patient was somnolent, and the pupils were moderately dilated and did not react to light. There was no effect on the pulse or respiration. An injection of sterile water did not show any results.

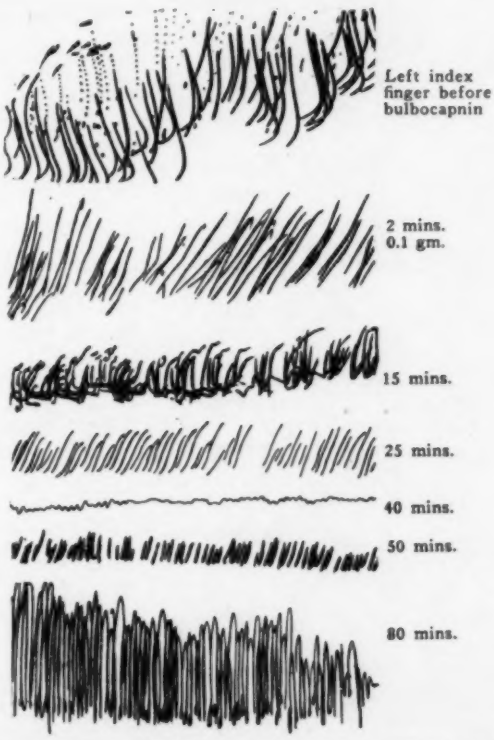

Fig. 5.—Case of postencephalitic parkinsonism. Handwriting after administration of 0.1 Gm. of bulbocapnine.

CASE 8.—*Examination.*—N. G., a woman, aged 54, had a parkinsonian syndrome, probably of idiopathic origin. Neurologic examination showed a masked facies; the pupils were slightly irregular, but reacted promptly to light and in accommodation. A marked tremor of all extremities, with increased tonus, was present. Although alert mentally, the patient showed paranoid trends and ideas.

Therapy.—After 0.1 Gm. of bulbocapnine was administered, a mild diminution of the tremor was noted. The pupils reacted promptly throughout the experiment. There was no change of pulse or respiration. The woman complained of dizziness and headache, and spontaneously stated that she was mentally dull. No records were taken.

The second group of cases studied consisted of seven patients with multiple sclerosis, one with Huntington's chorea and three with dystonia musculorum deformans.

CASE 9.—*Examination.*—In M. S., a man, aged 24, who had had multiple sclerosis for two and one-half years, the pupils reacted to light and in accommodation.

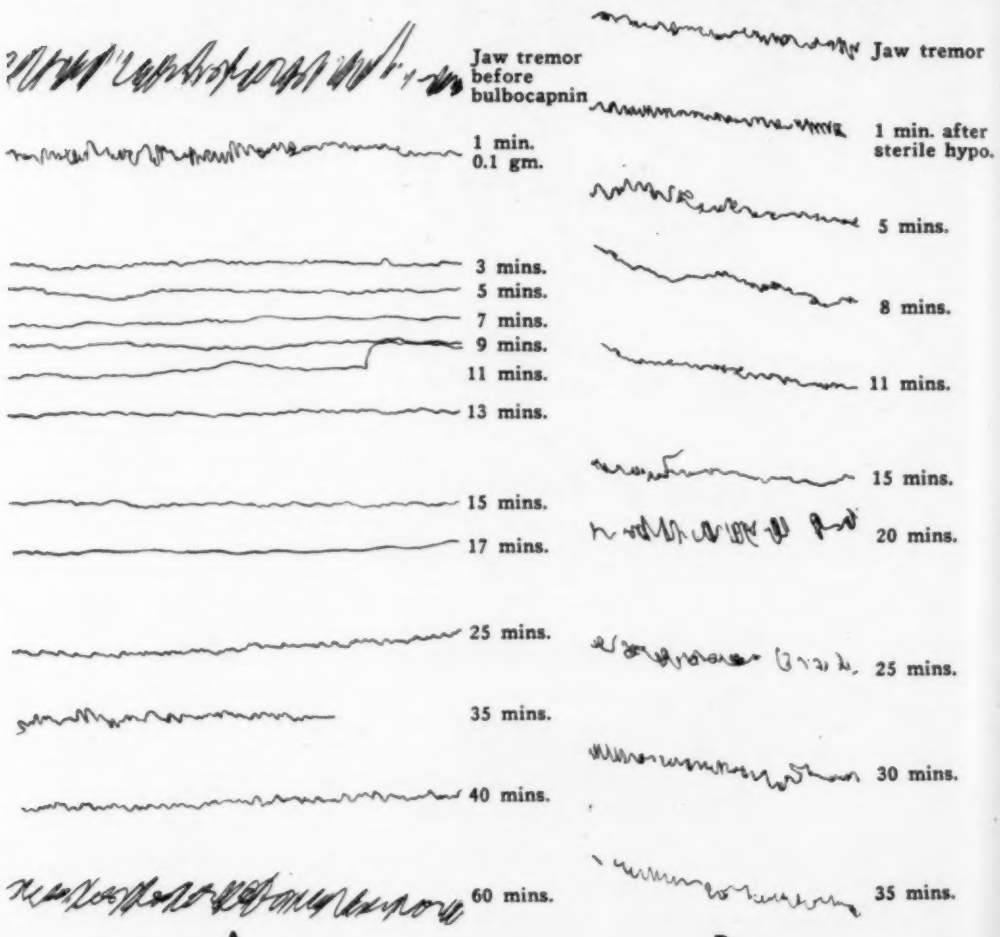

Fig. 6.—Case of postencephalitic parkinsonism. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine. *B*, handwriting after administration of sterile water. Tremor of the jaw was recorded in this case.

The speech was of cerebellar type. There was marked intention tremor of the right upper and lower extremity. The gait was of a gyric type. Signs of bilateral involvement of the pyramidal tract were present.

Therapy.—A record of this patient's writing was taken, and the intention tremor as shown by the finger-to-finger and finger-to-nose tests was noted. One-tenth gram of bulbocapnine was administered, and the effects were observed. The first

specimen (fig. 8 *A*) was illegible, and the individual letters could not be made out. The ataxia was marked. A gradual improvement took place and at twenty-five minutes the writing was distinctly legible, the word "Montefiore" standing out fairly clearly. There was a definite diminution in the intention tremor, the patient being able to touch his nose readily, a feat of great difficulty previous to the administration of the drug. This patient complained of severe dull frontal head-

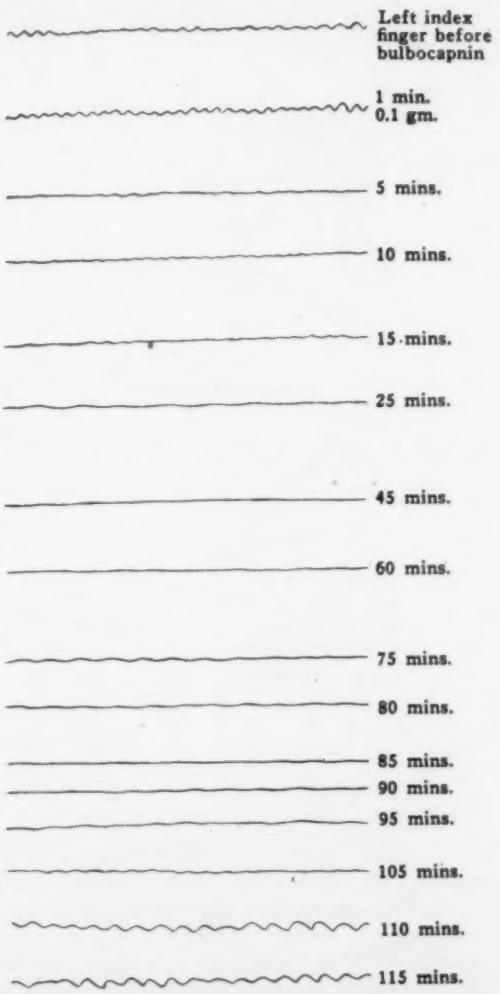

Fig. 7.—Case of postencephalitic parkinsonism. Handwriting after administration of 0.1 Gm. of bulbocapnine.

ache, dizziness, sleeplessness and dulness mentally. These after-effects were quite unpleasant, and the patient, an unusually intelligent young mathematician, complained bitterly. The pupils were in middilatation and did not react to light or in accommodation during the period from ten to thirty-five minutes after the injection, after which time they reacted promptly. The pulse rate was between 80

and 86, the respiratory rate, between 18 and 22. There was no effect on the scanning speech or the nystagmus. The control experiment several days later did not show any effects on either the writing (fig. 8 *B*) or the intention tremor.

CASE 10.—*Examination.*—In C. O., a man, aged 27, who had had multiple sclerosis for two years, the pupils reacted to light but not in accommodation. Nystagmus in all planes, scanning speech, intention tremor of both upper extremities, and a marked tremor of the head were present. A bilateral Gordon Holmes phenomenon, a cerebellar gait, generalized tendon hyperreflexia, and a bilateral Babinski sign were noted.

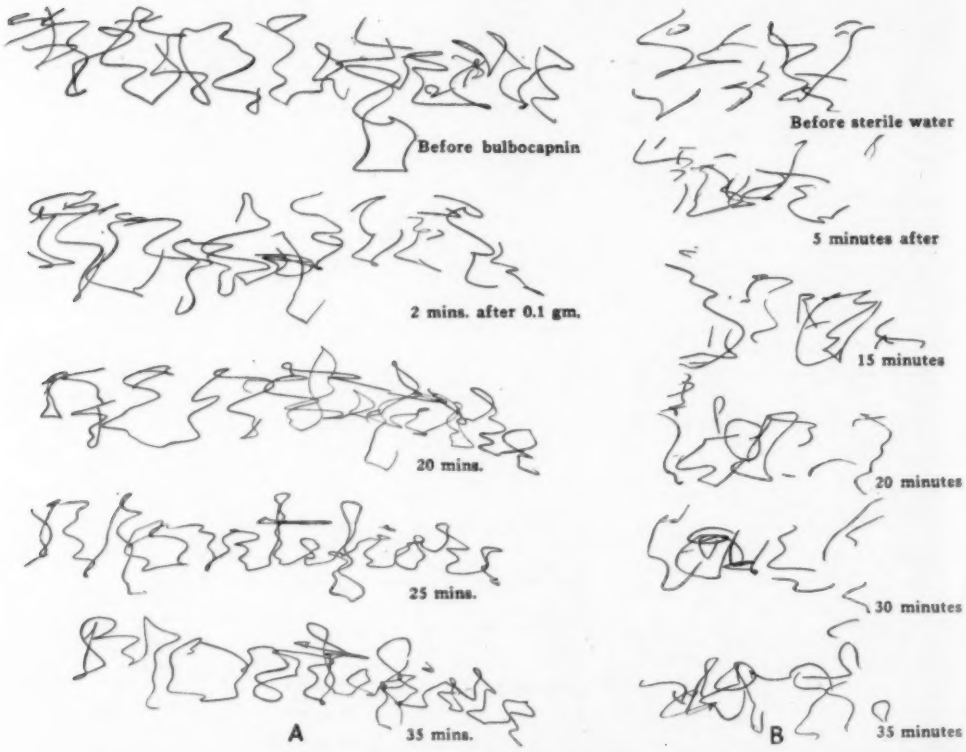

Fig. 8.—Case of multiple sclerosis. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine. *B*, handwriting after administration of sterile water. After the administration of bulbocapnine, the patient was able to write the name "Montefiore" more legibly.

Therapy.—A dose of 0.1 Gm. of bulbocapnine was given, and specimens of writing (fig. 9 *A*) were obtained. There was some improvement in the writing, as shown in the fifteen minute specimen. The intention tremor was slightly diminished but there was no effect on the tremor of the head, speech or nystagmus. As in the previous case, the patient complained of headache and dizziness. In addition, he was greatly fatigued with a feeling of heaviness in the limbs and sleepiness. The patient retired to bed, unable to cooperate any further on account of the intensity of these effects.

The specimens of writing (fig. 9 *B*) obtained several days later, when sterile water was administered, were distinctly more legible than on the previous occasion. The intention tremor at this time was also less marked. We cannot explain this.

CASE 11.—*Examination.*—In M. K., a woman, aged 26, who had multiple sclerosis, the pupils were slightly irregular, and reacted promptly to light but sluggishly in accommodation. A marked intention tremor was present, especially in the right upper extremity, with tremor of the head. The speech was scanning. Signs of bilateral involvement of the pyramidal tract and cerebellar gait were present.

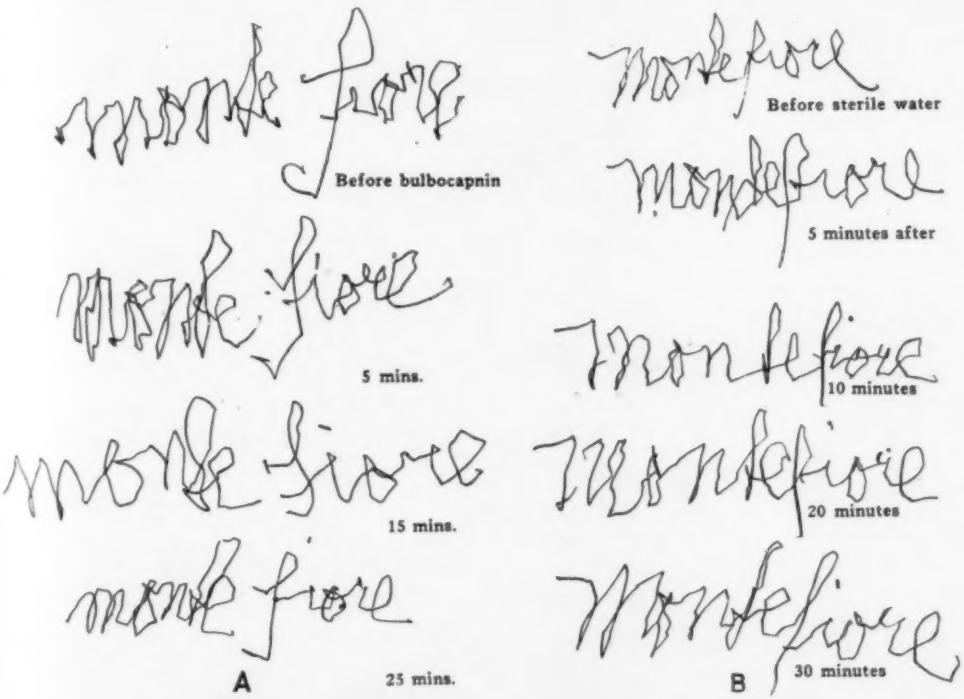

Fig. 9.—Case of multiple sclerosis. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine. *B*, handwriting after administration of sterile water.

Therapy.—One-tenth gram of bulbocapnine was given subcutaneously, and specimens of writing were obtained (fig. 10 *A*). The writing was legible in this case, but there was no free flow. The letters were angulated, and the ataxia was shown by the irregularity of the lines forming the individual letters. A slight improvement took place, gradually increasing to its maximum at about fifteen minutes. The letters became curved and distinctly more legible. At twenty-five minutes the ataxia returned and the thirty-five minute graph shows a return to the original state. In this case the headache was fairly well marked, and dizziness was a prominent symptom. There was no effect on the speech, tremor of the head or nystagmus. The pulse rate was between 86 and 92; the respiratory rate, 18 to 20.

A control specimen (fig. 10 *B*) showed a slight improvement in five minutes. This was only transient, however, the writing becoming gradually more difficult to decipher with increase of the intention tremor.

CASE 12.—*Examination.*—In A. H., a woman, aged 22, who had a multiple sclerosis syndrome, possibly on an epidemic encephalitic basis, there was a marked intention tremor of the right upper extremity. The cogwheel phenomenon was present with increased tonicity. Signs of bilateral involvement of the pyramidal tract were present.

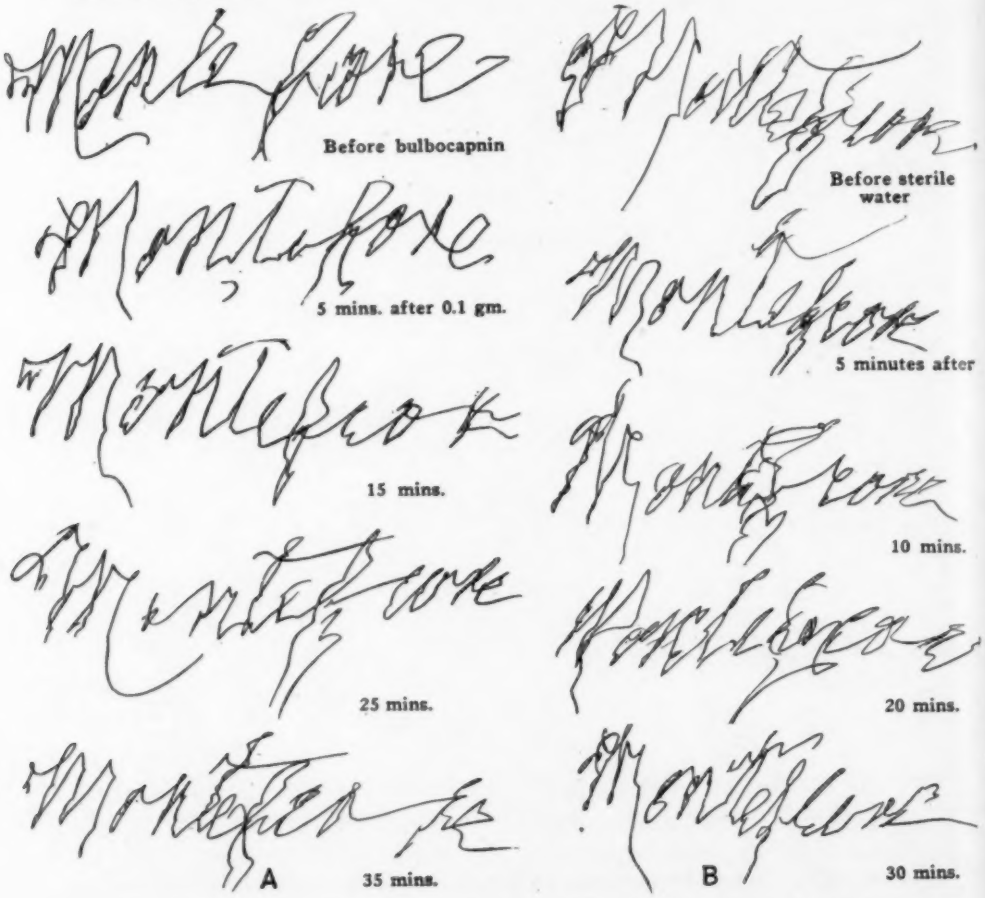

Fig. 10.—Case of multiple sclerosis. *A*, handwriting after administration of 0.1 Gm. of bulbocapnine. *B*, handwriting after administration of sterile water.

Therapy.—There was little effect on the writing (fig. 11), intention tremor or speech. The dosage in this case was 0.1 Gm. of bulbocapnine.

CASE 13.—*Examination.*—J. H., a man, aged 54, had had multiple sclerosis for twenty-one years. Neurologic examination showed a typical syndrome with a marked tremor of the head.

CASE 14.—*Examination.*—L. S., a man, aged 60, had had multiple sclerosis for eighteen years. General physical examination gave negative results. Neurologically,

he showed a typical syndrome with Charcot's triad. The pupils were irregular and sluggish to light.

Case 15.—*Examination.*—I. M., a man, aged 38, had had multiple sclerosis for nine years. Physical examination gave negative results. Neurologically, he showed a typical syndrome.

Therapy.—The three last cases in which the symptoms date back many years may be taken as a group. Each patient was given 0.1 Gm. of bulbocapnine. The intention tremor was so marked in each case that it was impossible to get specimens of the handwriting; the finger-to-nose test was used as an index of the

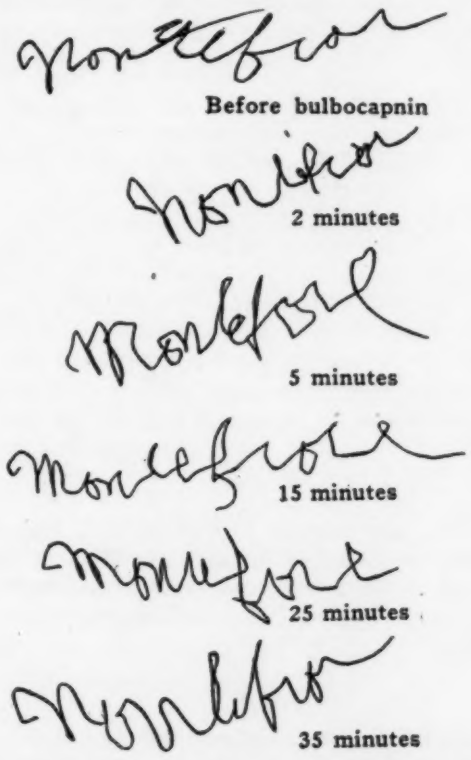

Fig. 11.—Case of multiple sclerosis, possibly postencephalitic type. Handwriting after administration of 0.1 Gm. of bulbocapnine. There was a slight effect on the handwriting because of marked intention tremor.

effects of the drug. In the three cases, in spite of a repeated dose at the end of twenty minutes, there was no effect on the intention tremor, nystagmus or scanning speech. All the patients complained of headache and dizziness, and one patient (case 14) became sleepy.

Case 16.—*Examination.*—In P. F., a woman, aged 24, who had had dystonia musculorum deformans for seventeen years, physical examination gave negative results. Neurologic examination revealed: the pupils reacted to light and in accommodation; the movements of the limbs were of the athetoid type and marked torsion spasm was present.

Therapy.—After the administration of 0.1 Gm. of bulbocapnine, the movements were definitely diminished. The patient rested quietly and was not sleepy. The pupils reacted to light. There was no change in pulse or respiration. The control experiment with sterile water did not show any effect.

CASE 17.—*Examination.*—In J. L., a boy, aged 16, who had had dystonia musculorum deformans for nine years, the abnormal movements were marked.

Therapy.—One-tenth gram of bulbocarpnine did not produce any effect. After a repeated dose in forty-five minutes the patient complained of drowsiness and slight headache, but there was no effect on the abnormal movements.

CASE 18.—*Examination.*—A. B., a woman, aged 22, presented a curious combination of choreiform, athetoid, dystonic and parkinsonian-like movements. Physical examination gave negative results except for pelvic inflammatory disease of gonorrheal etiology.

Neurologically, the pupils reacted to light and in accommodation. In addition to the abnormal movements mentioned there were some signs of involvement of the pyramidal tract. She admitted syphilitic infection; a Wassermann test was negative.

Therapy.—After administration of 0.2 Gm. of bulbocapnine it was noted that the gross movements disappeared for a period of forty-five minutes, only the finer parkinsonian-like tremor remaining. The patient was drowsy and complained of severe headache and dizziness. The pupils were in middilatation and did not react to light. The patient then went to sleep for one and one-half hours and when she awoke the abnormal movements were again present in full intensity. The pulse and respirations were not affected.

CASE 19.—*Examination.*—B. N., a woman, aged 37, had Huntington's chorea. Physical examination gave negative results. Neurologic examination revealed typical choreiform movements. The pupils reacted promptly to light and in accommodation.

Therapy.—After the administration of 0.1 Gm. of bulbocapnine, the patient was observed for a period of sixty minutes. There was a gradual diminution of the abnormal movements with the maximum effect between ten and forty minutes after the administration of the drug. The pupillary responses were normal. The pulse and respiration did not show changes.

COMMENT

Bulbocapnine seems to have a definite effect on abnormal movements in persons with dyskinesia. In the patients with paralysis agitans, this effect was marked in two, lasting for approximately forty minutes in one and seventy-five minutes in the other. The third and fourth cases showed some effect. Contrary to previous observations, it was found that in the encephalitic type of parkinsonism we were able to obtain definite results, as evidenced by cases 4, 6 and 7. The graphs are not entirely representative of the clinical results, as the effects were not of equal intensity in all the extremities, i.e., while the record of the index finger showed a total cessation of the tremor, the movements of the legs and jaws, although diminished, did not disappear entirely in some cases. There was no effect on the hypertonicity in the idiopathic parkinsonian group.

In the group of patients with multiple sclerosis there was definite improvement, with almost complete cessation of the intention tremor in case 9; in another, the improvement was relatively slight (case 12), and in two patients the improvement was noticeable but not marked (cases 10 and 11). In the three patients (cases 13, 14 and 15) whose symptoms were of long duration, improvement was not noted. In all the cases of this group there was no effect on the speech, nystagmus or tremor of the head. In the dystonic group we observed definite results in case 18, some quieting effect in case 16 and no effect in case 17. The patient with Huntington's chorea (case 19) showed definite improvement in the abnormal movements. There were no appreciable changes in the respiratory and pulse rates.

Observations of the pupillary phenomena were interesting. The dilatation and sluggishness to light noted in some of our cases were reported by de Jong and Schaltenbrand [3] in their work on apes. Headache and dizziness were found almost constantly: thirteen patients complaining of headache and eleven of dizziness. Nausea was a symptom in three cases. The hypnotic effects were also well marked in twelve patients, three of whom went to sleep. Five showed a definite dulling of mentality and one, fatigability.

It seems that the soporific effect of this drug may account for the diminution of the abnormal movements, as it is well known that these movements disappear during sleep.

It is of interest to note that in our controls gradations of the tremors occurred, a fact noted previously by other observers. The intensity of the tremors and movements varies considerably from time to time in these patients, different factors being responsible for this. The same patient may at one time present marked and at other times hardly any movements. Excitement, fatigue and conscious efforts must be considered in evaluating the effects of the drug.

CONCLUSIONS

Bulbocapnine has a modifying effect on dyskinetic symptoms of extrapyramidal origin. This depends to some extent on the length of time the patient has been ill. Further experiments will be undertaken in an attempt to grade the dosage, if possible, by administering the drug per os to allow for a more gradual absorption. In this way, one may be able to obtain beneficial results without the unpleasant features that arose from subcutaneous administration.

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3. Schaltenbrand, G. S.: Ueber die Bewegungsstörungen bei akuter Bulbocapninvergiftung, Arch. f. exper. Path. u. Pharmakol. **103**:1, 1924.

LYING AS A SOCIAL PHENOMENON*

IRA S. WILE, M.D.
NEW YORK

"Thou shalt not bear false witness against thy neighbor." This commandment is duplicated in form and spirit in almost every formulated religious and ethical system. Nevertheless, deviations from this ideal are so exceedingly common that many have said with the psalmist, "I said in my haste, all men are liars."

HISTORY

The history of man reveals interesting material concerning lying as a part of ordinary human relationships. There are many illustrations of varied angles to the subject: One may think in terms of Ananias, Jacob, Cellini, Falstaff, Baron Munchausen and Dr. Cooke. One may dwell on the unique Academy of Liars among the Gascons. One may think of Hermes as the god of lying. One may dwell on interesting anthropologic facts such as that Samoan children, like those of old Sparta, were taught to lie, and that the Arabs have a moral code that condones dishonesty and violence. Man lies in biology when he tells the story of the stork. There has been a long social sanction to lying in the legal formula caveat emptor, in commerce generally, in politics, in religious practices and even in the formulation of an oath to speak the truth. Society itself has recognized countless variations in the forms of lies, more numerous than those elaborated by Shakespeare in "As you Like It," wherein he refers to "the retort courteous, the quip modest, the reply churlish, the reproof valiant, the countercheck quarrelsome, the lie with circumstance, the lie direct."

It is my purpose to inquire into lying as a social phenomenon and to seek a rational explanation for the prevalence of this phenomenon and the attitude of society toward its general appearance and varied manifestations.

While man may be termed a psychobiologic unit, he may be more properly viewed as a biologic social unit. The conception of man is a social phenomenon as well as one having its origin in biologic urges. The birth of a child, lactation and the age of infancy, permitting the biologic evolution of the organism, is inherently social experience. The biologic organism, even though born spontaneously, could not live in vacuo nor separate from the community of man. The dependence on food, for example, calls for the social satisfaction of a biologic need, and

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the biologic satisfaction is a social essence. Part of man's biologic nature permeates his social life, and many of his social characteristics arise on biologic foundations.

GROUP VERSUS INDIVIDUAL BIOLOGY

One may, indeed, differentiate the biology of an individual from the biology of the group, just as one may distinguish the sociology of a group, paradoxic as it may sound, from the sociology of an individual. The biology of the individual is constituted by inherent natural biologic forces whether they be deemed physicochemical or endocrinologic, grossly material, or the result of vitalistic principles and even soulful creation. The mechanisms of life, movement, locomotion, secretion and excretion and reproduction, and the integrations of the nervous system thoroughly represent individual biology.

In the sense that a group has life and vitality, origin, optimum growth, possible decadence and death, there is a group biology. The life of a group contains analogous principles of movement and growth which give concern to the biologists who are interested, for example, in racial variation, differential fertility, population equilibrium and eugenics.

Group sociology is concerned with group relationships. Society is the interaction of component units with a focus of attention on the weal of the group rather than on that of the individual components of society. At no time is the entire individual absorbed by society. Sociology is a study of human relationships, whether the relationships of a universe of people or of a nomadic tribe, of a small rural semifixed community or of a family.

In contradistinction to this social organism there is what may be regarded as the individual element, which apparently consists of the individual projections that each unit of society permits to enter into the basic sum total of relationships that constitute the social group. Thus, an individual projects himself into a large variety of situations and has innumerable social contacts, willingly and unwillingly. The nursing child has a definite social dependence, a social content, a social acceptance, a social demand and indeed, although slow in learning it, a social obligation. Lactation represents the projection of the child's personal traits into another being, thus constituting a social relationship; this is one of the beginnings of society for an infant. The adolescent youth who is undergoing tremendous physiologic transformations, who is preparing to emerge from his pupal state into an imago is conscious of a vast variety of social relationships which are merely projections of his own personality. These social relationships, like his biologic alterations, possess marked lability and in consequence the adolescent youth

is in harmony or conflict with various social groups at different times for different reasons, and with different effects on himself both socially and biologically.

The larger the societal group, and the more complex its organization, the greater shrinkage there is of the individual value and the greater absorption of society in itself. Under these conditions a greater degree of liberty is possible for society because social truth becomes more difficult. Finally, there is some loosing of the social attitude, until individuals or society again feel some threat to their ego. Patently, at all times, however, the individual recognizes the protection which he secures through his group contacts and his social organization. If, therefore, individual reactions become too free and fail to take adequate cognizance of the social group, society as a whole begins to recognize a threat against itself. The threat against itself brings about a reaction against individuals, and the individual, in order to check again the hazards threatening himself, becomes more absorbed in the social phase of his existence, and finally may actually participate in pressures to bring about a limitation of his own course of action or thought.

In a sense, except for purposes of discussion, one cannot separate man's biology from his sociology in his practical living. Professor Cooley, in discussing social organization, referred to man as having two manifestations, one in individual life, and the other in social life, both being aspects of the same processes. One may extend this application from man almost to the totality of human experiential existence. Man is a biologic social microcosm.

As man does not live alone, it is obvious that the necessity for living together calls for shifts in response to internal needs and external demands. Man's organization complicates his socialization, and his socialization in turn affects his mode of organization. Man, alone, may be dominated by the absolutisms of his personal interest, but dwelling with others breaks down the absolutism and creates in place standards of conduct and behavior that actually condition the drives of personal instincts and modify the directions of habit formation. There can be little question but that man's nature derives its richest values from man's place in social living. Man's actions and thoughts, and one may even say his physiology and his psychology, are subject to variations incidental to the pressure of definite and indefinite social factors, such as those crystallized into the mores. The social psychologist is likely to conclude that man's thoughts, feelings, desires and impulses—in short, his higher mental activities—are actually derived as a result of social conditions. And there are those who believe that, in the last analysis, the instincts and emotions that form man's equipment are inherited merely by reason of their social significance. Regardless of this, it

cannot be denied that mental activities and mental life belong to a group as well as to an individual; that the mental life of the individual derives much from the group, and that it is the common contribution of the sum total of individuals that establishes the mental levels of society.

Social organization calls for the adaptation of self to the social demands. The biologic needs as well as the biologic structure of the individual definitely affect his personality and, indeed, help him to determine the degree to which he will accept or reject these social demands. The large problem of the individual in social organization consists in maintaining individuality in the face of the social pressures to which he must conform. There is ample evidence to indicate that lying may be a primitive type of performance for the purpose of giving the impression of conformity without destroying individuality. If, however, one assumes lying to be purely atavistic, it is apparent that lying has not lost its biologic values in acquiring social values. It is equally evident that the biologic and social values are applicable in turn to the individual and to the group.

It is obvious that in human organization friction is inevitable. Individual persons are concerned with their personal good, with the promotion, development and conservation of their egoistic trends. Groups, as a whole, are equally concerned with the maintenance and preservation of herd bonds and relationships, which may be and often are quite definitely opposed to the interests of specific individuals. Hence, there must arise definite social sanctions, which become crystallized into formulations, ethics, laws, codes, ordinances and the like, aggregations of regulations, of thou-shalts and of thou-shalt-nots. It is evident, therefore, that ethics is an organic phenomenon growing out of social needs standardized in the interests of the many, yet, theoretically at least, representing the welfare of each individual. I say theoretically, because practically these very laws and ordinances and ethical codes, which are sanctioned by the community and have frequently the additional power of accepted tradition, are not accepted by some egocentric persons whose consciousness of self appears transcendent to the consciousness of social relationships and obligations. Hence, just as ethics is rooted in the needs of society for cohesion, so crime is rooted in the nature of society as constituted by nonaccepting individualism. He who accepts ethics is socially minded; he who violates ethics is less cognizant of his social need than of his biologic make-up. It was probably an appreciation of the tremendous amount of egocentricity that led Plato to remark, "You cannot guide the multitude without deceiving them."

Racial habits are undoubtedly born of biologic needs. The essence of biologic activity is self protection. To this extent biology is con-

cerned with the pleasure principle. If lying is a social habit it undoubtedly is an outgrowth of individual biologic needs. A biologic need represents the organization of ego trends for the purpose of promoting safety, success, power, independence, recognition, dominance and the like; all of which serve life in its essential individuality. There can be little question theoretically that lying as a measure to bolster, support and enhance the ego would be esteemed as a virtue in oneself and deprecated in others. The very biologic benefits to the ego derived from lying would lead it to be regarded as a biologic reaction to be avoided and to be escaped from when manifest by others. Thus it is patent that while, biologically, lying advances one's own personality, the exhibition of this habit on the part of others in the same group would threaten the individual. In consequence, for the preservation of group relationships, lying would be frowned on, and truth would become the standard for group action. There would naturally be an exception to this principle, as lying by the group might promote the integrity, progress, strength and value of the group as a whole. Unity of idea and action would be harmonious only with a more or less homogeneous group. There is ample support for this biologic restriction of deception and falsification by a group standard.

BIOLOGIC NEEDS OF MAN

Individual Needs.—The biologic needs of man, whether considered as an individual or as a group, are definitely self centered. In the individual these biologic needs may be regarded as the concentrate of the ego instincts, but many biologic traits which are self protective to the individual are self protective to the group also. And the biologic needs are actually demonstrated in nature, where one finds special variations for purposes of self protection. Nature is guilty of lying for biologic purposes. The protective coloring of plants, the trickery of carnivorous plants and, indeed, even the securing of pollination through the satisfaction of the palate of an animal are indications that deception has definite biologic values. One need only think of the protective devices existent among animals, such as the form of the walking stick, the leaf butterfly and praying mantis, the color changes of the chameleon, the playing dead of the opossum, the simulation by the flies of the appearance of bees, butterflies and moths to realize further the biologic value of deception—nature employing numerous horrific forms to convey false impressions of power, strength and poisonous character. There is little difference between the cyst formation of the ameba, the feigning of death by a beetle and the syncope of a man on a battlefield. The dropping of a leaf or branch of mimosa on being touched, and the limping of a small boy simulating injury are biologically analogous.

Society with its aggregate of biologic organisms is conscious of its component units. Society can and does lie because its composition is largely of projections derived from individuals. Individuals or a group of them can profoundly alter society. In a sense, then, society becomes inferior for the time being, and may, for its own biologic benefit, compensate by utilizing lying to augment its position. The lie may exert pressure on its internal adversaries or even bring about the destruction of a portion of its own organic body, and the biologic individuals of the social group generally are sufficiently akin in their ideas, so that they do not actually oppose the social lie lest they lessen their own freedom to use the lie to meet their own individual needs. According to Brill, a lie is a direct or an indirect wish, or, as he remarked, "Lying is one of the defense mechanisms that help the individual out of difficulties." The lie does not have to be a direct or an indirect wish to be a defense mechanism. There are a large variety of lies, some of which get individuals into difficulties far more than out of them. The social significance of the lie must be estimated in terms of its biology and its social implications.

Natural living involves some degree of dissimulation as well as simulation. Man's ordinary contacts involve many of what are politely termed mental reservations, which mean only incomplete truth telling. Erasmus is alleged to have stated: "Christians should tell the truth but they need not tell the whole truth." There is an element of deception which is recognized as having compound biologic-social values both for the individual and for the group.

That there are definite biologic elements entering into lying is obvious from the fact that the use of alcohol and drugs and the effects of various diseases as, for example, encephalitis, loosen many of the biologic controls and diminish the social controlling influences. The normal expression of biologic activity is termed lying only when there is a social standard for the biologic activity. Thus it is obvious that the egoistic elements are considered in terms of gregarious trends. Conscience, so far as lying is concerned, is the contemplatation of biologic and social values in conflict.

Social Needs and Urges.—In addition to trends of the specific ego there can be little doubt that socialization depends on basic gregarious urges and needs, whether they are viewed as a herd instinct or as an acquired habit for the purpose of sexual mating. The very needs of man as a social being involve a taking over of some individual functions by the group. Among the hydroids, for example, there are definite divisions of the vegetative and reproductive functions. The individuals in the hydroid community exist biologically by virtue of the communal activity; the vegetative organism is not responsible for its own reproduc-

tion, nor is the reproductive organism wholly responsible for its own nutrition. Thus one finds that there is not merely an identification of the individual with the group, but an interdependence and biologic social organization of the individuals in the group. Spencer, discussing the hydrozoa, remarked, "We have still acquired proof that the individuality of the members is partly merged in the individuality of the group." This biologic concept is not far removed from the psychologic concept as stated by Stekel, "The Spirit of Time is only the sum total of the minds of individuals. Only the knowledge of the psychology of the individual can give us an understanding of the psychology of the crowd." Stekel's statement is not as true as that of Spencer, because a knowledge of the crowd also gives us an understanding of the psychology of the individual. In other words, the group and the individual have certain merged phases, both biologically and socially. One notes a further exemplification of the social expansion along gregarious lines in such definite social groups as the bees, ants, fish, birds and man. In all these groups there are definite biologic social survival values which cannot be underestimated.

While the social distinctions, characteristics and traits are said to be in the community they definitely emanate from individuals, but they are also constituents of the community itself as distinguished from the mere aggregation of individuals composing it. Primitive life, whether in animals below man or in man himself, is constituted of individuals all of whom are not wholly merged in the group. The variant in society is highly prized within limits, but only to the extent that the variation is accepted by society. Variation may spell death to the individual, or the prize of recognition may not be paid until the recipient exists in spirit only. Individuals, as such, set up private judgments against social authority while social authority seeks to perpetuate its judgments by taboos, traditions and morals.

Society is not a group outside of man. Without man the individual and his concessions, all social organization would be impossible. The group mind, so-called, is circumstanced and circumscribed by the voluntary projections of individual minds. Society thus is a synthesized, more or less coordinate system of individual minds interacting for the benefit of the group as opposed to the individual. Accepting this theoretic group mind, one can readily work out for society, as for individuals, such problems as arise from cognition, affect and their resultant activities.

Morality and social freedom imply movement, effort and change. In many ways during the ages past there have been incompatibilities between man's physical demands and his psychic adjustments. All too frequently man called on magic and demonology to explain his biologic

deviations from the social standards. Morality is not fixed; it grows out of group experiences and is subject to change. All too frequently morality is itself an atavism representing only conformity to tradition and custom. Man hesitates to violate his own past. Morality too has derived increasing social meaning. Primitive man had two standards of morality, one directed toward the needs and protection of his group, and the other directed toward the outside world. Too frequently this primitive trend is still observed, for example, in the moral differentials between various groups of the population united by specific interests. A single form of this is represented in the idea that there is honor among thieves.

Whether one discusses lies or any other form of reaction one must recognize that there is a distinction between a moral tradition and ethical conduct. Man in accepting social relationships loses a part of his individuality, and he may indeed be absorbed to complete passivity. The highest form of morality is that originating in voluntary acceptance of group needs for protection. One need not be as pessimistic as Sir Bamfylde Fuller who described morality as, "A petrifaction that has been formed in the springs of assertive volition." Man's greatest accomplishment lies in the self activity that permits him to be an independent thinking unit. Unfortunately, this state-of-being too frequently involves the acceptance of a social penalty that jeopardizes not merely his social esteem but his biologic achievement and satisfaction. There is a vast difference then between a practical morality which is concerned with the material consequences and an ideal morality that is attractive but rarely achievable, and the conventional morality that is more or less obligatory to save one's social face. Lying must be considered in connection with these variations of morality so far as they represent forms of social adaptation.

Classification of Lies.—It is evident, therefore, that there are distinct degrees of deviation from an absolute truth as well as marked variations in crudity. As an illustration one may say that there are definite refinements in lying and variations in the social codes, as exemplified in trapping elephants, ambuscades, duplicity, diplomacy and lies of convention, evasion and truth. This naturally leads one to inquire what constitutes a lie. If lying is a form of social adaptation, does it have the same natural history, so to speak, as lies for biologic adaptation? And if lying is a form of biologic social adaptation for the group, is it identical with what may be called lying for personal benefit as employed by the biologic social individual?

A lie is a consciously false statement to achieve certain results by the deception of others. It involves a consciousness of the falsity of the statement, an intentional deception and a distinct purpose in view.

Society, like any of its component individuals, must reveal these elements in its lying technic. One must distinguish lies told by the group as a whole or by sections of it. There is a vast distinction, for example, between lies for purpose of war propaganda dealing with frightful atrocities, accusations made against labor by capital or vice versa, or the allegations of Bolshevistic activity against every form of social legislation that is proposed. One need not mention the Avila papers as being more serious falsifications than some of the reasons that have been alleged by nations to explain or excuse their entrance into war or into a temporary seizure of a custom house. There are countless activities of society containing all the elements that I have enumerated as constituting a consciously false statement to achieve a certain result by the deception of others.

Society parallels individual activity in many ways by its reactions to swindling, cheating and perjury, and there is also a parallelism between the frequency, conditioning, persistence, nature and often extravagance of the lying as a phenomenon. Society, however, is less prone than the individual to acknowledge the error of its ways, and it is frequently only the historian who reveals the truth. Society all too frequently lacks that sense of shame, sin or guilt which reacts on the individual, because in society there is a sharing of the collective feeling and action and a sense of the necessity for social cohesion and protection.

Lies have been abundantly classified. Opie, 100 years ago, enumerated lies of vanity, of flattery, of convenience, of interest, of fear, of first rate malignity and of second rate malignity, the falsely called lies of benovelence, the lies of real benevolence, the lies of mere wantonness and the practical lies that are acted out. Burt's classification is more inclusive, involving the lie playful, of confusion, of vanity, of benevolence or revenge, of excuse, of slavishness, of loyalty and of convention, and the pathologic lies or mythomania. Each one of these forms found in the lives of individuals may be duplicated by analyzing group activity and the attitude of the so-called social mind in the expression of its social activity.

SOCIAL SIGNIFICANCE OF LYING

Lying virtually is not necessary for an isolated individual out of contact with his kind. Men do not consciously lie to themselves. Rationalization is an unconscious process. There are times when the individual justifies his action after the fact, but even so it is largely under the pressure of the desire for social esteem. Society, in a sense, constantly uses rationalizing processes. It is a phase of its own self-assertiveness. Society does not deceive itself any more than does an individual out of an interest in self-delusion, but because of a latent

undercurrent of reasonably conscious desire and a striving for self-respect, self-esteem, self-support, encouragement and maximation. Society, viewed as an individual, has an essence and this spirit is not in its existent consciousness, but is an imponderable element that serves as a substratum for social cohesion. Hence, society, like the individual organism, rationalizes its virtues and all too frequently ignores its vices or protectively rationalizes them as virtuous activities.

There is a measure of conscious lying in society in both the biologic and the social sense, just as one finds in the individual. One must remember that honesty or dishonesty and truth or lying do not constitute general traits. They are rather association reactions evidencing trends in action. Lying, like stealing, becomes a specific reaction whether manifest by one unit of society or by society acting as a unit.

The element of self enters into an individual action, and the element of self pervades social activity. All attitudes toward truth and lying are determined by the relations of these two ego principles. It is for the protection of these selves that rationalization exists. Society, like the individual, tends frequently to act from one motive and to make itself, as well as others, believe that the action has arisen from quite a different motivation. Society, with its habit formations, with its social opinion, which is thought, and its social sentiment, which is emotion, has nevertheless formed a reflex action based on primitive social organization. All these mechanisms are involved in the development of interest concerning activity, whether it grows out of the action of one or that of a multitude. Dr. Newman stated, "The Greek fathers thought that, when there was a justa causa, an untruth need not be a lie." This interpretation of the justa causa is too frequently the basis of social rationalization.

LeDantic asserted that the basis of society lies in egoism or self-interest; each individual behaves solely for his own benefit. The only reason for participating in social organization is to secure a defense against outward enemies, and in return for this service each individual concedes a part of his ego. The laws and customs of society, therefore, have grown out of organized self interest. While there is at present no thoroughly acceptable single theory to account for all the facts of human society, it is patent that "like-mindedness" is part of the essence of social thinking, social acting and social codes. The group relationship toward truth and lying, therefore, should represent the organization of thought and feeling for the cooperative good of the individuals comprising society.

Adler in "The Neurotic Constitution" remarked, "The love of truth too is sustained by the craving for security and belongs really within the sphere of our personal ideal, while the neurotic lie represents a feeble attempt to preserve appearances and to affect compensation." Here

truth is represented as the personal ideal, when, as a matter of fact, it is constituted as a group ideal for the uniform protection of all its members. The acceptance of the ideal by the individual is the only fact which tends to make it a personal ideal. The suggestion concerning the neurotic lie is applicable to all lies which represent attempts, feeble or otherwise, to preserve appearances and to effect compensation among other goals.

Protective Value of Lying to the Individual.—Lying is a specific reaction of social man for biologic and social values. The urge to lie arises from both the biologic and the social plane. There is a need to safeguard the ego in relation to the demands and pressures of the herd. Lying, therefore, is not a completely individual determinism, but then individual determinism is as impossible as social determinism. As Ellwood wisely remarked, "The individual and society are correlatives . . . and neither can be understood apart from the other."

Lying, in a way, constitutes a social escape from social disorganization. Truthfulness, honesty and sincerity are the foundations of social relationships; they form the binding mortar of the social structure. In every phase of conduct, activities have their dual relations to the single I and the multitudinous you. Individual morality may be higher than the morality of the group—the social morality. Group morality may be raised to a higher standard plane out of fear for itself. Group morality, as a whole, may be definitely higher than the morality of single individuals. On the other hand, the cross section of group morality is unlikely to be much higher than the average cross section of the morality of the socially bound individuals. Conceding these points of view, it is evident that society must tend to place truth on the pedestal of an ideal morality, even though it is conscious of the existence of lying in some form as a phase of practical morality. Not infrequently, the attitude of the social group toward lying is that expressed by Byron in Don Juan:

> "And after all, what is a lie?
> 'Tis but the truth in masquerade."

There is definitely a social inhibition directed toward lying. Frequently there is such a marked conflict between the biologic and social phases or values of a statement that a lie is tolerated instead of being repressed. And the individual in turn is frequently prone to tolerate the social lying as an evidence of his own self-submission to the regulation of the group and as an evidence of his complete identification with the group in the form of loyalty; for example, one can never see any wrong perpetrated by one's own family or nation. This form of acceptance of social lying by the individual grows out of a full consciousness of the participation of one's ego moiety in the social ego.

One finds the contrary ideas expressed in Ephesians 4:25: "Wherefor put away lying, speak every man truth with his neighbor; for we are members one of another."

Morality is organized inhibition that grows from prohibition. I shall not do, because I may not do. I do not wish to do, but if I must do, I do so willingly. A positivism lies in the ambivalence of the negation. Lies, for example, are frequently tolerated by a group because they represent loyalty to a group. The lie may grow from the loyalty, or the loyalty may grow from the lie. The height of morality is achieved when there is a fusion of the biologic and social values for man as a whole and man as an individual. This is, of course, part of the moral concept of a philosophic anarchism. In such a morality truth would have no terminology because it merely serves as an ethical basis of a current coin the obverse of which is falsehood.

Social Value of Lying.—Lying has social values, and social lies may be classified in part: as lies advancing the social self against outsiders; lies protecting society from its internal foes, and lies belittling others for the benefit of the social self. These same crude categories are applicable in an analysis of the individual lying. The social lies are of two general types. First, there are the aggressive, often called self defensive, conscious and deliberate efforts for the benefit of the group; second come the self-defensive lies involving concealments, flight from reality, half truths and denials. Society uses a deceiving mechanism to enhance its position or to gain profit, to increase its self importance at the expense of others, to gain in commercial competition, to bring about a greater consciousness of its own unity, to astonish outlanders with its own importance, to attract attention if only through exaggeration, to feed the social vanity, to develop ideas of strength or romance and at times even to foster persecutions in the form of false accusations. As in the case of individuals, the defensive lies growing out of a sense of fear are for the purpose of avoiding social punishment, to escape the disagreeable, to lessen a sense of inferiority, to serve social opinion and sentiment, to secure relief from the discommoding pressures exercised by members outside the specific group and to escape social disciplines by disguising one's intentions and purposes. It is unnecessary to illustrate these various types as they are almost self explanatory, and are the types that protect a social group against individuals or social groups not contained within itself.

Some forms of social deviation from truth that protect the group against itself arise from uncertainty concerning the realities affecting the group. Part of them are in the nature of social fancy and fantasies, while many are the result of social imagination and the confusion of past memories with present necessities. And the social fantasy contains the same

element of pretence and make-believe, designed to promote the social escape from reality. It is a form of social invention for the purpose of manipulating aggressively or defensively concrete experience. Propaganda within the group frequently belong to this category of lying.

The form in which social prevarication is directed toward the external groups varies in method and purpose as requisite for promoting internal social welfare, diminishing threats to social harmony, for shielding innocent or guilty third parties, for promoting loyalties and at times for advancing what appear to be generally helpful larger social developments. There is little doubt also that at times there is a definite intellectual value in this externally directed social lying. It may be compensatory for intellectual weakness within the group or slowness in adjustment, for the purpose of augmenting itself, or as a mode of expression of what may properly be called social mental conflicts born out of social fears, greeds, angers, disgusts and similar emotions.

In general, one may observe that the principles involved are identical whether one lies for the purpose of protecting society as a whole, recognizing the expansibility of the term society, or whether one thinks in terms of a small section of the earthly group, of the affairs of a city or a nation or of the activities of a sect or a lodge. When a state denies the existence of bubonic plague or foot and mouth disease, it is in little different category from a community that suspends a school superintendent on the grounds of insubordination, when it is merely because of the political activity of an Anglophobe mayor. The social taboo of sex makes the stork a symbol of social fear and social falsity. The alibi tendencies of a community and the status of perjury are no more significant than the magnification of a national hero, indicating his greatest virtue to be that he never told a lie. Society then, through aggressive and defensive types of activity, seeks to maximate its ego and assuage its sense of fear. In this maximation there can be little question concerning the social sanction, whether on the basis of worship of success or admiration of virtue.

It is apparent, however, that such forms of social protection are designated in the interest of the mass and are utilized by smaller or larger unit groups without consideration of the right of the individuals. As Kidd commented, "The claims of the clan entirely swamped the rights of the individual." Early society had a morality within the clan, and the strongest relationship was a consanguineous relationship. These distinctions of social bonds still exist. Lying to one's family is more reprehensible than lying to one's neighbor. Freud, in contemplating the psychology of the group as the oldest human psychology, conceded that, "What we have isolated as individual psychology by neglecting all traces of the group, has only since come into prominence out of the

old group psychology, by a special process which may still perhaps be described as incomplete." It is evident, of course, that individual psychology must be just as old as group psychology. From the beginning, man has had the two phases to which I have referred, and these are more or less responsible for the psychology of the unit individual and the multiphased psychology of the unit individual in his various unit groups. This statement is made without accepting Freud's theory of sexual jealousy and individual envy as the basis of social organization and group psychology.

I have commented on the fact that the ninth commandment is represented in various codes, social and moral. Buddha's command was, "Thou shalt not lie." Confucius, among his five cardinal virtues, mentioned sincerity which includes truth. Truth represents an ideal of social relationships. It is an absolute constituent of social morality. Just as the individual recognizes the value of falsity as an escape mechanism for himself, he appreciates his protection by the truth speaking of all others. The multiplication of this individual idea serves to place it within the category of principles acceptable for social cohesion. Society accepts this projected individual value of truth and makes it its own.

The truth is an ideal, a socially protective device. The concept of truth socially contains the pleasure principle so far as truth, accepted as a quality of the mass, yields a sense of social security and satisfaction in the release from imminent threats. There are times, of course, when pleasure is attached to the social lie just as an individual may find a satisfaction in his successful lying, whether it is interpreted as shrewdness, sagacity, smartness or merely "putting something over." This content of social satisfaction is often realized in the presence of a broad hoax, a literary joke or an April fool process. There is, indeed, an appreciation when the lie itself does not deflate society, lessen its power or diminish its authority. Since truth is part of the content of most social ethical formulations, it is evident that man's reasoning power has clearly defined his ideals. Experience indicates, however, that there has ever been a real conflict between the absolute theory of life and the practical attainment of the ideal goals. Truth is an ideal still unattained. The highest forms of social groups undoubtedly hold lying in contempt. There are still large elements of exceedingly practical but less ideal social organizations that would merely state that honesty is the best policy. Lying, with its social sanction, possesses a narrow view in which the emphasis is on success, achievement, bringing things to pass, adding to the reputation or beneficial profit of a larger or smaller group that represents a self-conscious portion of society. Truth, however, is held as an ideal by society, because lying typifies a breach of social promise,

is a threat to social security and is deemed an act of cowardice growing out of fear. And yet all these may be recognized as having values for self protection.

REACTIONS TO LYING

Reaction of the Individual and of Society.—The social reaction to lying is aroused in proportion to the effect of the lie on social welfare. Captain Koepnick who can deceive a community brings the form of recreation that Barnum recognized. The more a lie simulates truth and the less hazard it presents to the group the surer it is of nonrejection. Laughter converts a violation of truth into a joke, thus fundamentally giving the lie another type of sanction. There is a definite degree of social indifference concerning falsification when danger does not exist. A lie may be received with contempt or even with good nature. It is significant that the approach to the simulation of truth is only a step below that category of lies that are never found out, on the principle that what you don't know does not hurt you. There are times indeed, when lying may almost be regarded as a virtue; as Fairbairn remarked, "The lying which is held to be better than the truth is a lie that is not found out." If, however, group safety, comfort or happiness is threatened, lying is rebuked or condemned. If the lie carries with it a marked threat to social welfare, there is a danger to the perpetrator, whether an individual or a group.

Our moral ideas are not biologic, but are acquired by social heritage. They arise directly and indirectly through and from social contacts. Today our social attitudes may be regarded as social formulations by men over man, with variations depending on time, place and circumstance of the group. There is, thus, the definite interaction of the individual who is striving for place and power, for life and comfort in terms of his desires and for potentials in the face of the organized society of which he is a part, but which has different objectives than he, because it is concerned with all of its members. Society seeks to use man, as is natural, as an element of its own organism, to secure greater strength, energy, potencies and favors for its own enlarging social self.

The standardized individual attitude toward the lie, then, is the result of actual experience plus the direct and indirect experiences of society. The interest in truth, therefore, possesses the dual values of self interest and social interest. The individual is cognizant of biologic and social values in lying, and consequently makes many modifications of his behavior in view of the communal pressures in behalf of the biologic and social values of the group. The individual projecting relationships are in turn influenced by the relationships with which he is in contact.

SOCIETY'S UTILIZATION OF THE LIE

Society has not hesitated to utilize the lie as a form of social strategy possessing definite survival values. Society, as a whole, has made use of lies of concealment for protection, lies born of selfishness, lies in the interest of social friendships and loyalties, and lies for the purpose of fostering wars and for securing peace. Society with an anthropomorphic conception of God has not hesitated to lie to a, or the, God or to an Olympus of gods. Society has frequently justified the breach of truth in its own interest.

One thinks of the dying Jew having his name changed in order to deceive the Heavenly keeper of the Book of Life. Definitely religious lies have had justification in a Jesuitical principle. In the words of Lecky, "The Fathers laid down a distinct proposal that pious frauds were justifiable and even laudable, and if they had not laid this down they would nevertheless have practiced them as a necessary consequence of their doctrine of exclusive salvation."

Credulity encourages lies and credulity is a marked characteristic of man and his society. Credulity stimulates liars. Society has not hesitated to lie to outside social groups as, for example, bearing false witness against the Gentiles, or Spartan lying to the Barbarians. In the medieval ages, lying was an acceptable trait and virtue of the chivalrous knight. Society has not hesitated to falsify statements concerning unfavored minorities, whether single individual reformers or groups who might appear to threaten disorder. Social lying, in a sense, may be regarded as being a natural response toward all threats against the social order. Dynamic progress, unless definitely revealed as aiding society, comes under the ban and opprobrium is heaped on it regardless of its truth. Society has no hesitancy in its reversion to primitive cruelties in crushing whatever arouses its fear or suspicions. The lie is one of the social instruments.

It would seem apparent that the lies of children or adults should be interpreted only in terms of the social setting. It matters little whether the form of lying is a direct misstatement, a simple false accusation or a pathologic mythomania. A lie has a combined biologic and social element and should be studied in the light of both of these pictures. The adaptations of individuals and communities are to a large extent similar. The very changes in growth and development bring about the necessity for readjustment. Adaptation involving a balance of forces may be regarded as the practical achievement of a mobile equilibrium. Adaptation involves a balance of external natural and social forces in combination and interaction with the internal inherent reflexes and acquired habits.

Social lying with its various counterparts in individual lying presents an opportunity for interpreting man's place in nature and his integrated responses to the total stimuli which condition him. There is also possible an appreciation of society's place in nature and in relation to its component individual units in their struggles for existence. If one recognizes that man uses society as a lever on his environment for the sake of his personal adjustment, one must also see that society utilizes man as a lever on the total environment for social protection. I would suggest a schematic presentation of the place and relationships of an individual in the universe.

First, let us conceive a tremendous hollow sphere containing all nature. It is indefinite in extent, unlimited in power and definitely affecting man and society biologically and socially. In this natural sphere, the perimeter is a solid layer that contains all the elements of climate, meteorology, earthly topography, mountain and valley, ocean and bight, flora and fauna, light, heat, moisture, and other conditions, the powerful influences of which are recognized.

Secondly, let us conceive within this sphere another smaller sphere that, for the sake of brevity, I shall term human society. This sphere is peculiar in that it is not a tangible organization. Nevertheless, as social environment it involves all of the social instruments including law and government, economics and education, traditions and mores, ethics and, in part, religion. These are now the forces that enter into man's social heritage and help to determine his reaction as an individual seeking to become a socialized being.

Thirdly, let us try to conceive man as an atomic character just outside the surface of the social group, between it and the limiting sphere of natural resources and forces. In harmony with his distant relative the ameba, he is capable of protoplasmic projections. His social biologic organization calls for sustenance, support and contact, and he projects parts of himself until they come in contact with large numbers and varieties of projections that have emanated from other individuals like himself. The intertwining, interweaving and intermovement of the projections constitute the origin and sap systems of society.

INTER-RELATIONSHIPS BETWEEN MAN AND SOCIETY

Individual man has his own biologic structure and mechanisms. His physical organization and characters involve his endocrine system, his neuron patterns, his visceral systems and their coordination, all the essential reflexes, natural and conditioned (in other words all the biologic machinery the potentials of which constitute both the content and the method in pursuit of certain life goals). In addition, he possesses a special power that is termed intelligence, by which I mean his innate

inherited capacity to learn, together with his imagination, his creative power, his normal abilities and disabilities which enable him to function with understanding and sympathy on a higher than vegetative plane. He also possesses systems the natures of which are still in doubt, that are termed emotional. The nature of these emotional systems in his conscious and unconscious life provides much room for conjecture and investigation.

Man, therefore, in this scheme, would appear to be constantly in contact with the environment of relationships and the environment of nature both of which he is seeking to influence, affect or control for his individual benefit and for the benefit of his social group. In every sense, man's projections into society constitute his part of his own social environment. This is the center of the theory of circular response. In the words of Follett, "Beyond the effect of organism on environment and environment on organism, the organism responds to the relation between itself and environment. Any analysis of behavior which does not take into account that response is to a relating, will be inadequate. Any analysis of society which does not take into account that response is to a relating, gives us the determinism of the last century."

Inherent in this form of relationship between the individual and the group is the possibility for relational traits to develop through and include imitation and suggestion which are the main factors in promoting human adaptations. These two processes not only aid society in bringing about conformity of individuals and in promoting uniformity in mindedness, but also set up the background for individual thinking. It is patent, therefore, that with the growth of society, the individual must benefit, and, from the usual developments of the individual, society should benefit. Participation in group life is part of the individual experience, and interest in individual living tends to enrich the community.

While biologically, then, man would appear in my schema to be an individual set apart functionally, he is integrated to a large extent with the very relationships in which he is only in partial contact. I should not go so far as to say with some social psychologists, "The individual as we know him has been developed as part of a larger life-process; in other words, is largely a social process." The individual develops too many variations physically and mentally and makes too many advances for the social group to be regarded as merely a social product. His biologic organization has definite values that are apart from the contacts with society. The disease of a single endocrine organ affects the nature of the individual too extensively to be put aside in a consideration of man's individual life and in terms of his special projections. This also obtains for such conditions as toxic states and infections.

Another suggestion that grows from this form of organization is that the man without his relationships may be regarded as a bundle of ego traits, instincts or self-centered characteristics. So far as he projects himself and, by his projections of self constitutes a social organism, he establishes his herd tendencies and traits, or characters that constitute his gregariousness and forms the basis of his sympathies. I may say in this connection that sex, ordinarily regarded as a biologic instinct and urge, must likewise be regarded as a social instinct and urge. I regard the sex pressures, urges and drives as a mechanism utilized by and for the ego and by and for the herd. In its essence, a social reproductive measure has definite ego values. Thus most of the conflicts regarding sex arise from this distinction between individual and social biology, individual and group social values.

Possibly I can clarify this schema in another manner. Consider that each individual mind projects itself thus toward and into the social group in which it finds itself, as this is essential for the recognition of the existence of the group. The sum total of these projections then constitutes a confederated mind which has a common value and use in maintaining the integrity of the social mind and even as a means of protecting and safeguarding the minds from which the constituent projections have emanated.

If one will conceive not merely a stimulus and response reaction of the individual to society, but of an oscillating wavelike movement constantly acting between the individual mind and its projection, one can appreciate the nexus between the individual mind and the so-called group mind. If, for example, a condition arises which concerns more particularly the welfare of any group as a whole, as against any individual, it is patent that the projections will convey such a message to the individuals who thus feel the need of reacting in terms of self protection, though virtually they are reacting in terms of what the group regards as essential for the welfare of the group. It is equally obvious, therefore, that there can be various shifts in group attitudes and reactions which may run counter to other forms of group reactions, depending on the particular social group of projections and the ends and aims of the groups thus constituted. Society at large would, therefore, be an integration of various lesser groups with varying strains, pulls and pressures.

Each individual is reasonably free to enter more thoroughly into social thinking, or to withdraw completely from it as a whole or from any part of it.

It is incorrect to say that the moral ideals of the individual are wholly determined by the group consciousness. The individual may make a definite impress on the consciousness of his age and the morality

of his times. The moral status of a community at any time is, in a sense, the result of the interacting projections of the individuals. The morals of the people, therefore, cannot rise above its sources. The morals of the group, however, should not be regarded as merely the sum total of the moral ideas of the constituent social unities. The moral ideas of the group are determined by the needs of the group as distinguished from the needs of the individual. Truth is more essential to the group than to individuals and hence the paramount place of truth in ethical codes.

If, therefore, lying exists as a social phenomenon, it exists because a social need for it is believed to exist; it must have its part to play in the social code. There are some characteristics of social behavior that ordinarily would belong to an individual endeavoring to inflate itself or protect itself. This would obtain regardless of whether these egoistic trends are the result of development from an animal level of psychology.

The ideal moral code of a community represents the ideal line of activity when the individual consciousness is represented in society not merely by a slight projection but by a fusion and an identity. The ideal code makes the interest of the social organism and of the individual identical. Under such circumstances only would the ideal be attainable and truthfulness become a de facto practice rather than a frequently ignored ideal.

Assuming life to be merely a manifestation of energy, there is no difficulty in accepting the principle of partial identity of the individual mind and the social mind. I am not concerned at the present time with the mode of development of the social conscience and whether it is due to suggestion, imitation or instinctive development. The existence of waves in the air capable of interpretation into sound, speech and music would have been regarded as folly had there not been disclosed a wave cycle that could be utilized so that the voice and ideas of Europe and America could be interchanged by radio. One may, by analogy, regard the social conscience as a continuous interweaving of individual waves. At no time is the complete individuality of any one in the air. Yet the sum total of idea waves abounding in the universe may represent a potent influence on society itself. The very potency of radio has an inhibitory force. This potential individual and social wave may be a medium for bringing humanity into closer accord. It thus becomes a social instrument for morality. Just as the individual broadcasting may affect the waves that may reach others, so in turn is he, as listener, under the influence of what he hears or refuses to hear.

Man's behavior and conduct are determined by conscious and unconscious factors. Just as one speaks in terms of an individual conscious-

ness and unconsciousness one may refer to a group consciousness and a group unconsciousness. In many ways, the discussion of instinct, reflex, habits and intelligence as applied to individuals has its analogies in social existence. Regardless of how man seeks to escape by stressing his individualism, he is indubitably a part of society, whether he wills it or not, although he may determine the extent and depth of his contacts and the degree of firmness in his own relationships. Man's consciousness is projected to society and the collection of these related projections constitute social consciousness. What people term social contact is only part of the social projection. Individual thinking and contemplation of social relationships in itself constitute another phase of social conduct.

Many contrasts exist between the individual and society. There need not necessarily be strong antagonisms. Social consciousness is evidenced in part in social opinion, and social feeling or sentiments reflect this essence toward single beings. Society consciously seeks for itself just as do individuals. Society can only use the projections that the individuals supply; yet the social consciousness can work against single individuals by the introjection of the integrated projections. Society can only build up its conscious life and method to the extent that the individual consciousness accepts in conscience the basic ideals of the socially conscious group as applicable to itself. Hence, there are two sets of ideals. Only thus is it possible to recognize the principle of freedom for man and freedom for society. The social consciousness then becomes individualized and thus unified on some common interest as race or religion, fear or vanity. The social consciousness as a unit exhibits its instinctive tendencies, reflexes and habit forms just as does an individual.

As man, in my hypothesis, is born a biologic social unit, his consciousness and unconsciousness must take cognizance of all the social implications of its biologic growth. At no phase of life is there social discontinuity. Conception and birth are social phenomena; so are death and the ideas of the hereafter. Social fusion and biologic union are probably coordinate in time, and the conscious and unconscious processes result from the simultaneous exposure of the biologic and social phases of man to life experience. Unconsciousness and consciousness, whether of the group or of the individual, probably originated at the same time and have the two sources of growth on the basis of unified experience. Thus, then, biologic life depends on social contacts, and consciousness and unconsciousness are phases of biologic activity. The fact that animals herd together and react in manifold gregarious manners indicates the basic character of social phenomena. These traits are better exemplified in the mode of life of bees, ants, fish, birds and

mammals. The reactions in all of these zoologic families indicate a social consciousness which by many is explained on a biologic basis. One might even go so far as to grant that a social element is not alone an expression of biologic forces, but even conditions the biologic basis of life. Even the principle of eat or be eaten contains a social significance as well as a biologic motivation.

When the principle of projection and introjection is considered, one has a two way system within the self, which has both conscious and unconscious phases. There is a relation between these two moieties that enter into human activity. The ameba moving about comes in contact with food and engulfs it, thus projecting itself on its environment. But when the food morsel appears for some reason to be unsatisfactory, and the pseudopodia of the ameba slowly release the particle of food or disgorge it, there is evidence of a simplified introjection. The environment has affected the ameba. The same principle may be extended and applied to the relation of man to society in terms of conscious and unconscious activity.

According to Freud, the group spirit is derived from individual envy. He argued that when individuals come into a group their individual inhibitions fall away, and all the cruel, brutal and destructive instincts which lie dormant in the individual as relics of a primitive epoch are exposed for action. He regarded the group spirit as revealed in the mob as a manifestation of this unconscious in which all that is evil in the human mind is contained as a predisposition. This means that the primitive man interpreted as a beast has its survival in every individual and serves as the basis of social organization. This point of view does not appear wholly reasonable, particularly when the sex implication of the envies are appreciated and rejected.

If man has a struggle between his biology and his morality, his personal war must be carried over to his group; and group morality, in a sense, must war with its own group biology. If society is based on envy and if a desire for equality in leadership is the binding force, then the elements in envy are free to act; thus fear and even rage enter to justify social lying.

While there need not be essential unities between the goals of man, the biologic individual, and man, the social individual; nor need he, as a whole, have the same objectives as all of the groups to which he belongs; nevertheless, he is functioning as a partially dependent cell in an organism, regardless of his individual specific functions. J. S. Haldane phrased this idea: "Just as the behavior of the cells in a combined organism is unintelligible, if they are considered one by one apart from their relations to the whole organism, so the acquisition of knowledge and conscious activity in general are unintelligible from the point of view of the individual man."

A catalytic process is constantly going on between what may be termed man's mind and the social mind. There is an ever present tendency to establish a balance between individual desires and social desires as manifest on the one hand by a personal goal and on the other by the social mores. The individual seeks to go ahead rapidly while society tends to go forward slowly. This need for balance helps to explain the varied waves of attitudes that are constantly disturbing the social seas. If the dynamics of mind are considered there is a constant movement of energy to and from man and society. Their relations are not static; their conscious positions are subject to change, and their unconscious relations give rise to social rationalizations on the same principle that they are serviceable individually.

The type of unconsciousness that I am referring to is not strictly in harmony with Jung's collective unconscious, because the collective unconscious of Jung is regarded as essentially unmoral. The moral law is developed for the main part in the individual by virtue of experience and training, by willing and unwilling acceptance of social pressures affecting his social trends and motivating to no small extent his biologic needs. The moral law forms part of the content of social consciousness, and much of it is relegated to social unconsciousness. Society can play the beast as well as can man, without making allegations of primitive impulses arising wholly in the sphere of the unconscious. The conscious and unconscious of society and of man contain elements that are creative and destructive, elevating and degrading, but always having definite survival values for the group as a whole.

CONSCIOUS AND UNCONSCIOUS SOCIAL VALUES AS APPLIED TO LYING

Let us consider, then, the implications of the conscious and unconscious social activities as they more definitely apply to the phenomenon of social lying.

I have stated that society is an intangible federation of organized relationships; that man as a biologic and sociologic organism has dual interests; and that society similarly has its own biologic and social ends which are not essentially identical with those of its component units. The ego motifs belong to biologic man, and the herd motifs to social man. The sex motif is a combining and synthesizing urge which in turn uses and is utilized by the ego and the herd tendencies. The herd has as great an interest in sex as the ego because it depends on it for its own continuity and growth. The sex motif does not serve as the reason for social organization, nor is it essential for individual growth and development. While the sex factor may enter into many forms of social lying, the lie should be regarded rather as an instrument of

aggression or defense, but always as an escape from a relationship, biologic or social, and most usually social.

Lying by its very nature requires two persons. Social lying frequently concerns a group as opposed to the individual. Social lying involves a conflict between the interest of the group and either the biologic ego or the herd relationship of the individual. These principles appear to hold true whether applied to the lies of individuals or to social lying. In another sense, the lie may be regarded as essentially a defensive mechanism to maximate the ego of the group. It may be reasonable to interpret it in the adlerian sense as an expression of the will to power, forming again a defensive mechanism for the relief of a social inferiority. At any rate, the lie is essentially a maximating fictitious adjustment—fictitious because the adjustment is not wholly on the plane of reality. A fabrication, social or individual, frequently calls for a compounding and pyramiding of lies in order to sustain the truth alleged in the lie.

It is apparent that social lying has both an aggressive and a defensive phase directed either against an individual or a group and reacting in favor of society as a whole or of the special unit group within the social organism.

I have already said that the individual unit is conscious of his own projections into social relationships, and it is the recognition and consciousness of this projection which give life to social consciousness. Social consciousness thus represents the summated projections of a group for self development, guidance and protection. An individual's recognition of communal participation with its self protective and self-advancing values constitutes an identification with society. If the recognition concedes only an incomplete identity of the group desires and interests with personal desires and interests there may be a social or an antisocial personality developed. If the identities are accepted as complete, the ego of the individual becomes completely absorbed as a social being, with almost a fusion of being through the complete loss of initiative and leadership. This type of person accepts by imitation, suggestion, reasoning and emotional reaction the complete domination of human relationships, without remonstrance or regret.

The essence of society inheres in the reactivity of individuals. The social reactions of individuals, however, are not identical with their biologic needs and performances except as there arises a psychosocial unity that is analogous to the psychobiologic unity.

The individual as a reacting system responds to his complete environment which acts as a stimulus. This response is not limited to individual isolated stimuli, but is an integrated reaction against the sum total of stimuli impinging on his biologic mechanisms at any one time. The

individual, however, so far as he environs himself, and because he is a part of his own environment, has a circular response to his own attitudes. The biologic effects of all these stimuli are significant. Another form of reaction, however, arises from the stimulation of his social reacting system, of which he also forms a part. These reactions are definite and powerful even though the group of social relationships may be regarded merely as a loosely bound agglomerate that can disintegrate into smaller groups under slight strains.

Society, like man, is biologically and socially responsive, and likewise biologically and socially stimulating. Society is both cause and effect, and man cannot escape either of these influences.

The infant begins life already projected into the world of relationships. He is not thoroughly cognizant of his own social contacts. His biologic urges are stronger than his social urges and his ego impulses dominate all social reactivity. Children are essentially nonsocial so far as dominant trends are concerned until they are willing to accept social responsibility, a sense of which does not really develop until late in adolescence. Marked evidence of truly overt social behavior is only slightly evident before the age of 3 years, and frequently is initiated by a period of negativism. The mere fact that there is no external expression of social attitude does not mean that it is nonexistent. There is in the child a recognition of this social obligation. Just as a child acquires a sense of appreciation of words heard long before he speaks, so there is an absorptive appreciation of relationships before an external evidence of its existence. The fixation of social reactions takes time, and is in fact what is ordinarily termed the process of socialization.

The young are still struggling for the preservation of individuality largely on a biologic plane without sufficient recognition that the social phases of individuality are aids in the preservation of the biologic elements as well. It is a struggle for the preservation of the self that brings about the conflict born of aggressiveness or the absorption due to passivity. And lying constitutes part of the combat for the preservation of individuality during the time that social relationships are slowly being established and more slowly being accepted. It is for this reason that lying in its various crude forms is more common among children than among adults. Throughout life lying continues but it is modified because of social requirements in order that individual conduct may be acceptable in terms of the group norm of conduct. In this sense lying does not mean untruth, error or fantasy, but only conscious, direct purposeful deception, as earlier defined.

SOCIAL AND ETHICAL VALUES OF THE LYING PHENOMENON

Social and ethical attitudes underlie all important reactions of the individual. It is these social attitudes that are responsible for the back-

ground which gives rise to a sense of sin, guilt or inferiority. The individual reactions are based on conflict of the ego principle with the herd ideal. Thus it is evident that society not alone determines its group ideals but sets up the machinery to determine the individual reactions toward them. Society provides the basis of crime, delinquency, eccentricity and other elements in a legal and social sense. Out of the social standardization of reaction grow the concepts of good and bad and of right and wrong. If lies are tolerated, condoned, or disregarded, it is because of a social concept in which is involved consciously or unconsciously the biologic survival values of the lie. The reflection of this social attitude must definitely affect the individual reaction. Hence, the lie as a defensive mechanism is thoroughly defended under different circumstances and conditions. One recognizes in social terms the white lies, the lies of courtesy and the lies of convention.

Lying, however, so far as it is evidence of conflict, may crystallize in a social form as the exhibition of a social neurosis; even nonneurotic individuals may be caught up in it. For example, at present, there are those who deny the validity of the Volstead Act on various grounds that they actually know to be false, and considerable social excitement is set up by the conflict between society's demand for respect for law as self protection, and personal contempt for legislation which limits the freedom of individuals in the community. Many people who never drank before prohibition are finding themselves caught up in the conflict.

The neurosis is an unconscious biologic social lie and escape; hysteria is an unconscious form of biologic lying socially fixed; while a psychosis is a social lie biologically fixed. These three terms may be applied with reference to social activity. One may make a partial application of these principles to individual reactions, although I shall not discuss them at length. A hallucination is a form of biologic lying by self projection. A delusion is a form of social lying because it is measured only by the social status of the victim and by the traditions, customs and beliefs of his age. One may divide neurotic forms in terms of biologic and social introversion. The hysterias may be regarded as biologic escapes of an ego from pressures of the herd. It is because sex values are tied to both the ego and the herd impulses that sex conflicts arise and may issue in the form of various types of social lying. This would adequately explain, for example, the escape value of the taboo.

Writing many years ago on the intellectual development of Europe, Draper remarked, "The constitution of man is such that, for a long time after he has discovered the incorrectness of the ideas around him, he shrinks from openly emancipating himself from their dominion; strained by the forces of circumstances he lives a hypocrite, publicly applauding what his private judgment condemns." This is the essence of social

lying. One recognizes that orderly living requires some degree of self subordination. Social control lies within the individual, although it is expressed in social rules, regulations, opinions and sentiments. Custom reflected back to the individual from whom, in fact, it emanated, acquires the force of a convention, and adverse judgments concerning it are difficult to secure.

Lying has thus far been discussed generally without any inquiry as to its ethical values. It may now be asked, Is lying right or wrong? Is it right or wrong individually or socially, either or both? Darwin was a strong supporter of the idea that the strongest organic motives are the instincts of self preservation and preservation of the species. Socially applied this would mean that the preservation of the group life is the main concern of individuals. Hence, all conduct of the individual or the group may be interpreted as good or right so far as it tends to preserve or increase the richness and depth of life of the community. Any conduct that would tend to lessen or injure the group life would, therefore, be deemed wrong or bad. Spencer similarly regarded ethical conduct as that which is conducive to the welfare of the individual, his family and the human race. That conduct is most ethical which benefits all individuals or combinations of individuals including the total group. This ideal, however, can only be reached when there is a fusion of the interest and ideals of the individual and his social group. Then, in the words of Spencer, "General happiness is to be achieved mainly through the adequate pursuit of their own happiness by individuals, while reciprocally the happiness of the individual is to be achieved in part by the pursuit of the general happiness."

A social concept of ethics is found in the language of Lester F. Ward, "Virtue is an attribute of life and character consistent with the preservation and continuance of man on earth. Vice is the reverse of this, and is felt as an attack upon the race."

A definition of ethics in the dictionary states, "Ethics is the voluntary conduct of a self conscious person, so far as that action is amenable to a standard obligation imposed on him by social influence or by a supreme plan of life that draws its material from society," or in brief, "Ethics is a system of rules for regulating the actions and maintenance of men in society."

Social lying then, if it exists, must be interpreted in terms of both the ethics and the mores. If acquired characters are not inheritable, society must repeat its moral struggle in every generation, and the moral code depends on the needs of the individual as served by the group. Likewise, the moral code of the individual is part of the social instruction by the group, and the practices of lying, as they exist, are reflective of the attitudes of the group in practical living. As Fairbairn

remarked, "What is in man is not independent of what is without him, but repeats and reflects it, lives in him in active intercourse with what is above and around him, just as his organism lives within and through its environment, absorbing into itself the elements without that are needful to growth and health within."

Jeremy Bentham interpreted right conduct to be such as results in the greatest good to the greatest number. If this is assumed as a legitimate interpretation of right, social lying must always be judged in terms of its causes, its mode of expression and its results. It is obvious that in this phase of the subject individual judgments may vary considerably from those of the group. In the long run, however, it is the group decision that prevails.

Morality is not biologically inherited. The social direction and guidance, the social standards and the social practices determine the status of lying as a principle of action. Society must, therefore, recognize lying within limitations as a form of conduct which promotes the adaptation of man to his environment. Goodness depends on the social opinion as to the degree with which the lie fosters the better adaptation of man in the society to which he belongs, with all its incompleteness and lack of harmony with individual objectives. Finally, one must view lying as an action from the angle of John Stewart Mill: "Actions are right in proportion as they tend to promote happiness, wrong as they tend to produce the reverse of happiness. By happiness is intended pleasure and the absence of pain; by unhappiness pain and deprivation of pleasure."

Under all these definitions of ethics, the right and the good, there remains the single social implication that human activities should be judged in terms of the group. Man with his colossal egotism, who pronounces the strongest mind the best and who has fostered the belief that might makes right, is not an independent spirit. He is held in leash by the thoughts, feelings and the activities of groups of men. When man lies, he is but acting out of fear and in order to secure some personal benefit or advantage. He has the moderate sanction for his act in the practice of society which is fundamentally the authority for and the basis of social lying.

The modern tendency to renounce cant and hypocrisy may raise the individual standards of truth sufficiently to affect the group ethics. Let us hope that in time truth may prevail and that the truth will make man free.

INTRACRANIAL TUMORS

A REVIEW OF ONE HUNDRED VERIFIED CASES*

CHARLES E. DOWMAN, M.D.
AND
WILLIAM A. SMITH, M.D.
ATLANTA, GA.

In classifying intracranial tumors we have adopted the suggestion of Cushing that the cases be grouped as follows: (1) tumor of the brain, verified; (2) tumor of the brain, unverified; and (3) tumor of the brain, suspected. In the first group are placed only cases in which the tumor has been seen, either at operation or autopsy, with the exception of gliomatous cysts from which xanthochromic fluid has been obtained by puncture. In the second group are placed cases in which the observations definitely indicate an intracranial tumor, although the tumor has not actually been seen at operation or autopsy. In the third group are placed cases in which the symptoms and observations lead one to suspect a tumor until the lesion is proved something else or until it is verified later as a tumor.

The cases on which this study is based have been taken from the verified group. For convenience in calculating percentages, 100 consecutive cases have been selected. From the standpoint of minute pathology the study is not complete, as only a small number of the tumors have been reviewed by the methods of Bailey, Penfield and others. We have had to retain the term "perithelioma" pending further study. It is our purpose, however, to stress in this review the clinical aspects rather than the operative technic or the microscopic structure.

The 100 tumors included in this study occurred in the following locations: frontal, 10; cribriform, 2; precentral, 18; postcentral, 8; temporal, 11; occipital, 2; chiasmal, 10; cerebellar, 18; pontile, 1; falx, 2; pineal, 2; ventricle (lateral), 1; cerebellopontile angle, 7; corpus callosum, 2; multiple, 6.

SYMPTOMS AND SIGNS OF CHRONIC INCREASED INTRACRANIAL PRESSURE

In practically all cases of intracranial tumor there occur symptoms and signs that indicate increased intracranial pressure and do not necessarily have any localizing significance. The degree of increased pressure depends as a rule on whether the tumor is above or below the tentorium. The increased pressure may occasionally be caused by the

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* From the Piedmont Hospital and the Steiner Ward for the Study and Treatment of Malignant Diseases.

tumor per se. As a rule, however, it is due to interference (by the tumor) with the normal circulation of the cerebrospinal fluid from the ventricles of the brain to the general subarachnoid space. We have analyzed these so-called general symptoms and signs and have learned that at times they may have certain characteristics of localizing value.

Headache.—Headache was complained of, at some time or other, during the course of the disease in 81 cases; in 37 cases it was the first symptom. The character of the headache was variously described. In general it was dull and diffuse or throbbing; although it was constant in some cases there were frequently long periods of freedom from pain. In some cases, the headaches eventually ceased entirely, in one case for the period of one year. Cessation of the headaches, however, never occurred in the cerebellar cases. In 10 per cent of all cases the headache was worse at night. Sharp pains in the head occurred in a few cases, and were the outstanding symptoms in a right lateral ventricle tumor. This patient would be seized with terrific sharp sudden pains of momentary duration. A change of position would frequently bring them on. A psammoma of the right choroid plexus was found at operation; the tumor had a pedicle which permitted it to change it position and we believe that a change in posture would cause the tumor to lie over the interventricular foramen, thereby producing an acute hydrocephalus. The pains ceased after removal of the tumor. Sharp pains at the vertex on movement of the head were present in one case of cerebellar tumor. Sharp pains occurred in the ears on movement of the head in a case of pineal tumor. There were similar pains in the occiput in an angle tumor. In a case of pineal tumor, there was a feeling of pressure at the root of the nose and a feeling as if an iron plate were lying inside the skull.

It was an old belief that the localization of the headache had some localizing significance. This may be true occasionally, but is not of sufficient constancy to be of particular value. As an example, the following localized headaches were noted: Frontal headaches were present in tumors of the frontal, cerebellar, precentral, postcentral, cerebellopontile angle and in the pituitary and pineal regions. Left frontal headaches were present in a left occipital and a left angle tumor. Pain behind the eyes was frequent in both cerebral and cerebellar tumors. Pain in the right eye was noted in tumors of both the right and the left parietal lobe. Bitemporal headaches were noted in frontal, cribriform, temporal, cerebellar, pituitary and angle tumors. Occipital headaches were present in 20 per cent of frontal, 9 per cent of temporal, 5 per cent of precentral and 60 per cent of cerebellar cases. There were no headaches in 19 per cent of the cases; they were absent in 20 per cent of frontal, 16 per cent of precentral, 12 per cent of postcentral, 28 per

cent of temporal, 50 per cent of occipital, 10 per cent of chiasmal, 28 per cent of cerebellopontile angle, 50 per cent of corpus callosum, 50 per cent of falx tumors, and in only 5 per cent of cerebellar cases.

Vomiting.—In 54 cases, there was a history of vomiting. Projectile vomiting is considered a frequent symptom of increased intracranial pressure. In only 11 of the 100 cases was there a history of projectile vomiting. In three cases, there was nausea without vomiting. Vomiting occurred in cases of tumors of various locations. It was less frequent in tumors of the temporal lobe (18 per cent) and most frequent in tumors of the cerebellum (90 per cent). In only 10 cases was vomiting associated with headache. In 2 cases, vomiting was the initial symptom noted; in both the tumor was located in the posterior fossa and in one of them vomiting had occurred daily for three years.

Visual Disturbances.—Although edema of the optic disks is one of the most frequent observations in intracranial tumors, the patients may not complain of poor vision until definite atrophic changes have taken place. One is often surprised at the visual acuity when, on ophthalmoscopic examination, marked choking is noted. When the vision becomes markedly impaired, the atrophic changes are so advanced as materially to affect the eyesight even after the pressure has been relieved. When total blindness has occurred, as a result of choked disk, a return of sight seldom takes place, even though the tumor is removed. This is not the case, however, when the blindness is due to direct pressure on the optic nerves. In 1913, for example, one of us (C. E. D.) operated on a patient with pituitary tumor (not included in this series) who had been totally blind for ten days. In this case, there was a retrobulbar optic neuritis with only slight primary atrophy. Twenty days after the operation, the sight returned and rapidly came back almost to normal. In the 100 cases, 53 patients complained of poor vision when first seen; of these, 12 were completely blind in one or both eyes. The visual acuity was not always the same in both eyes, one eye even becoming blind in some cases before there was much disturbance in the other eye. In the 12 cases in which blindness occurred, the time that elapsed between the onset of poor vision and complete blindness varied from three weeks to twenty-seven months.

The ocular fundi were normal in 14 of the 100 cases (1 frontal, 4 precentral, 3 postcentral, 2 pituitary, 2 cerebellar, 1 pineal and 1 temporal). In the remaining 86 cases there were positive observations as follows: (1) congested retinal veins only, 4 (1 precentral, 1 postcentral, 1 cerebellar and 1 multiple); (2) slight choking, 11 (1 frontal, 2 precentral, 2 postcentral, 1 falx, 2 temporal, 1 chiasmal, 1 cerebellar and 1 multiple); (3) marked choking (i. e., above 3 diopters), 55 (6 frontal, 2 cribriform, 8 precentral, 3 postcentral, 6 temporal, 2 occipital, 15 cerebellar, 6 cerebellopontile angle, 3 multiple, 1 falx, 1 ventricle

and 2 corpus callosum); (4) atrophy without choking, 14 (1 frontal, 2 precentral, 2 postcentral, 1 temporal, 1 cerebellopontile angle and 7 chiasmal); (5) arteriosclerosis only, 2 (1 postcentral and 1 precentral); (6) retinal hemorrhages associated with choked disk, 28.

One of the most valuable localizing diagnostic aids is a study of the visual fields. This was done in 81 of the 100 cases. The form field was taken as a routine, but the color fields were taken in only a few cases. In 6 there was total blindness and in the remaining 12 the patients were either unconscious or unable to cooperate in the examination. In 16 cases the visual fields were of localizing value as follows: (1) homonymous hemianopia, 6 (3 temporal, 2 occipital and 1 multiple [1]); (2) bitemporal hemianopia, 4 (3 chiasmal and 1 cerebellopontile angle [2]); (3) nasal hemianopia on one side, 2 (2 chiasmal); (4) temporal "cut-off" on one side, 4 (3 chiasmal and 1 postcentral).

When visual hallucinations occur they have localizing significance, particularly when the images are seen always on the same side. It is generally believed that complex visual hallucinations indicate a temporal lesion, whereas mere flashes of light indicate an occipital lesion. It is rather interesting to note that a history of complex visual hallucinations was obtained in only one of the 100 cases, although there were 11 lesions of the temporal lobe in the series. These hallucinations occurred in a patient who had a dural endothelioma under the right temporal lobe. She complained of seeing an automobile above the tree tops, the hallucination always occurring to her left. In the two cases of tumor of the occipital lobe, there was a history of flashes of light in only one of them. Definite visual hallucinations did not occur in any other case.

Diplopia is not infrequently complained of in cases of chronic increase of intracranial pressure. Of all the cranial nerves the sixth has the longest course within the cranial cavity. General increase of pressure easily affects one or both of them with a resulting imbalance of the external ocular muscles. It was noted in 34 of the 100 cases and had no localizing significance (except in 1 case of homolateral tumor of the pons) as is evidenced by its occurrence in tumors of the following locations: 2 frontal, 1 cribriform, 2 temporal, 4 precentral, 2 postcentral, 1 occipital, 11 cerebellar, 2 chiasmal, 1 pineal, 1 cerebellopontile angle, 1 corpus callosum, 1 falx and 1 multiple. Diplopia due to other ocular palsies was not noted.

Epileptiform Seizures.—The history of convulsions, particularly when they begin in adult life, should always lead one to suspect tumor of the brain as a possible causative factor. Thirty-nine of the 100 patients gave a history of having some type of epileptiform seizures.

1. In this case there was a tumor of the right optic tract.

2. In this case there was markedly increased intracranial pressure and dilatation of the third ventricle which probably produced direct pressure on the chiasm.

The attacks in 21 of these (54 per cent of all having seizures) had features of localizing significance. The attacks varied in type as follows: (1) Generalized attacks, 19 cases (4 frontal, 3 precentral, 2 postcentral, 1 corpus callosum, 1 temporal, 1 falx and 2 multiple tumors). In 2 of these cases, the attacks continued to be generalized for from eight to twelve years after which they became localized. In 3 other cases, the attacks were followed by localized weakness (1 temporal, 1 precentral and 1 cerebellar). In 2 cases the attacks were preceded by hallucinations of smell (1 temporal and 1 chiasmal). (2) Jacksonian attacks (from the start), 14 cases. These attacks consisted of either localized jerkings or of localized numbness. They occurred in cases with tumors located as follows: cribiform, 1; precentral, 6; postcentral, 2; falx, 1; angle, 1; temporal, 1, and multiple 2. In 1 case with a precentral tumor the attacks began as jacksonian but later became general. (3) Tonic seizures, 2 cases (1 cerebellar and 1 cerebellopontile angle). (4) Unconscious attacks without convulsive movements, 4 cases (1 cribriform, 1 temporal, 1 pituitary and 1 corpus callosum).

Mental Disturbance.—Varied mental disturbances were noted in almost one third of the 100 cases. Although in some cases mental symptoms might be interpreted as being caused by an increase of intracranial pressure, we believe that in many cases they are of definite aid in localizing the tumor. There were mental disturbances of some type in 31 cases (8 frontal, 7 precentral, 2 postcentral, 6 temporal, 2 cerebellar, 3 chiasmal, 1 cribriform, 1 corpus callosum, and 1 lateral ventricle tumor). If we group the precentral cases with the frontal (the precentral area is in reality the posterior part of the frontal lobe) and also include those tumors which pressed on the frontal lobe (chiasmal and cribriform) we find that of the 31 cases, the tumor involved the frontal lobe in 17, the temporal lobe in 6 and the corpus callosum in 1. This leaves only 7 cases in which the tumor was located in other regions. Marked drowsiness was noted in 2 chiasmal cases and was probably due to a disturbance of the vegetative centers in the floor of the third ventricle. This leaves only 5 cases of the 31 in which the mental disturbance could be strictly attributed to the general increase of intracranial pressure. The various mental disturbances noted are shown in table 1. True motor or sensory aphasia, word or object blindness, hallucinations of vision and smell and astereognosis have not been classed as pure mental disturbances. We are convinced that in the chronologic development of symptoms the earlier the mental disturbances the more likely is the tumor to be located in the anterior part of the cerebrum.

Vertigo.—Attacks of dizziness were complained of in 29 of the 100 cases (6 cerebellopontile angle, 5 cerebellar, 5 temporal, 4 postcentral, 1 occipital, 2 chiasmal, 2 multiple, 1 frontal, 1 precentral, 1 pineal and 1

lateral ventricle tumor). The vertigo was associated with a staggering gait in 5 cases. Dizziness suggests a disturbance of the vestibular pathways and should be more pronounced in tumors located below the tentorium. This was true of cases under observation, although the dizziness occurred in tumors of other locations, particularly the temporal and parietal lobes. In only 2 cases was the vertigo made worse on motion of the eyes or change of position.

Loss of Smell.—Loss of the sense of smell was noted in 10 cases. A unilateral loss of smell occurred in 5 cases (2 precentral, 2 temporal and 1 cerebellopontile angle), and a bilateral loss of smell in 5 cases

TABLE 1.—*Mental Disturbances in Cases of Intracranial Tumor*

Type	Number of Cases	Location of Tumor
Memory disturbance	10	5 frontal 1 precentral 2 temporal 1 corpus callosum 1 cerebellopontile angle
Disorientation	3	3 frontal
Apathy or lack of interest	3	2 frontal 1 cribriform
Conduct disorder	2	2 frontal (one patient was eccentric and the other would go half clad)
Drowsiness	11	1 frontal 1 cribriform 3 precentral 1 postcentral 2 temporal 2 chiasmal 1 cerebellar
Childishness	3	1 frontal (constant use of mirror) 1 cribriform 1 chiasmal
Sphincter indifference	7	5 frontal 1 cerebellar 1 corpus callosum
Narcolepsy	3	2 precentral (patient would go to sleep while talking) 1 suprasellar cyst
Difficulty in thinking	2	1 frontal 1 lateral ventricle
Feeling of unreality	1	1 precentral
Disturbance of calculation	1	1 temporal
Fits of temper	1	1 postcentral

(2 cribriform, 1 precentral, 1 corpus callosum and 1 multiple). In these cases, this symptom had localizing significance in 2 tumors which occurred above the cribriform plate and therefore actually involved (through direct pressure) the olfactory bulbs, and also in 2 tumors of the temporal lobe in which there was a homolateral loss of smell.

A loss of both smell and taste on the same side may occur in a lesion of the uncinate gyrus, as described by Spiller,[3] but this was not noted in any case of this series. It was present in one of our unverified chiasmal tumors.

Dilated Veins of the Scalp.—Localized dilatation of the veins of the scalp was noted in 5 cases (3 frontal, 1 postcentral and 1 cerebellar).

3. Spiller: Uncinate Syndrome, Arch. Neurol. & Psychiat. **16**:73 (July) 1926.

The dilatation occurred in the frontoparietal region and was on the same side as the tumor in all cases. Three of the tumors were endotheliomas, and 2 were gliomas.

Blood Pressure.—It is assumed by some that tumor of the brain causes an increased blood pressure, but our observations do not confirm this. In table 3 the blood pressure readings are recorded as taken at the first examination in 78 cases. In only 11 cases was the systolic blood pressure over 140 mm. of mercury. Seven of these 11 patients were over 40 years of age.

Pulse Rate.—There was a bradycardia at the time of the first examination in only 1 case; this patient had a terminal medullary compression. The pulse rate in 82 cases is given in table 4.

TABLE 2.—*General Symptoms of Intracranial Tumors*

Symptom	Percentage of Occurrence	Percentage of First Symptom
Headaches	81	37
Vomiting	54	2
Visual	53	5
Convulsions	39	10
Mental	31	1
Vertigo	29	2

TABLE 3.—*Observations in the Blood Pressure in One Hundred Cases*

Systolic Blood Pressure	Number of Cases
Below 100	8
100 to 110	13
110 to 120	22
120 to 130	16
130 to 140	8
140 to 150	4
150 to 160	2
160 to 170	1
Over 170	4

Roentgen-Ray Observations.—In 40 of the 100 cases, abnormal roentgen-ray observations were noted. In 17 of these there was convolutional atrophy, due to an increase of intracranial pressure of long standing. These changes which are usually most marked in the frontal and temporal regions were noted in tumors of the following regions: 1, frontal; 2, precentral; 2, postcentral; 2, temporal; 5, cerebellar; 3, multiple; 1, falx and 1 in the corpus callosum. A thinning of the posterior clinoid process was noted in 1 tumor of the temporal lobe and 1 tumor of the cerebellopontile angle. In the remaining 21 cases the roentgen-ray observations were of definite localizing value, as follows: There was complete disappearance of the normal sella turcica in 7 cases (all chiasmal). There were areas of calcification in 9 cases (2 frontal, 2 precentral, 1 temporal, 3 chiasmal and 1 pineal). Localized thickening of the skull was present in 2 cases (1 precentral and 1 frontal); in both of

these there was an underlying endothelioma. A shift of the pineal shadow was noted in 1 case (precentral). There was a notch in the region of the internal auditory meatus in 2 cases (both acoustic neurinomas). This particular abnormality was not sought for except in recent cases.

In 20 cases a ventricular injection of air was undertaken as an aid in localizing the tumor. This examination was made in 1 frontal, 2 cribriform, 2 precentral, 1 postcentral, 4 temporal, 1 occipital, 3 cerebellar, 2 pineal, 2 corpus callosum and 1 lateral ventricle tumor. The ventricular puncture was not followed by air injection as shown by roentgen-ray studies in two of these cases. In one, the needle entered a large tumor originating in the splenium of the corpus callosum. There was an escape of blood from the needle which was then withdrawn. The patient lived several weeks after an unsuccessful exploration, and the location and character of the tumor was determined at autopsy. The other patient was a girl who had become totally blind, and the

TABLE 4.—*Observations on the Pulse Rate in One Hundred Cases*

Pulse Rate	Number of Cases
40 to 50	1
60 to 70	8
70 to 80	8
80 to 90	22
90 to 100	19
100 to 110	14
110 to 120	1
120 to 130	7
130 to 140	2

location of the tumor was uncertain. The right lateral ventricle was punctured, and there was an escape of a tremendous amount of ventricular fluid under great pressure. The patient went into collapse and died a few hours later. At autopsy, a large glioma in the left temporal lobe was found. The left ventricle was completely collapsed and there was a large fresh hemorrhage in the tumor. This had evidently been caused by the shifting of the brain at the time the fluid escaped from the greatly distended right ventricle.

In the remaining 18 cases the following observations were noted: (1) bilateral hydrocephalus with obstruction of the interventricular foramen (determined by two separate examinations) in 1 corpus callosum tumor; (2) bilateral hydrocephalus with patent foramen of Monro in 3 cerebellar, 1 pineal and 1 lateral ventricle tumor; (3) collapse of 1 ventricle in 1 frontal, 3 precentral, 1 postcentral, 3 temporal and 1 occipital tumor; (4) collapse of 1 anterior horn in 1 cribriform tumor; (5) collapse of both anterior horns in 1 cribriform tumor, and (6) shadow of the tumor superimposed on normal lateral ventricles in 1 pineal tumor (the shadow of the tumor was also brought out by the air in the lateral ventricle tumor and in the other pineal tumor).

When the ordinary roentgen-ray studies were combined with those following ventricular injections of air, the roentgen-ray examinations gave valuable localizing aid in 39 of the 100 cases. In 4 of the 18 cases studied with injection of air there was enough neurologic evidence to warrant a localizing diagnosis. In the other 14, however, the air studies were essential for localization.

Studies of the Wassermann Reactions of the Blood and Spinal Fluid.—In 20 of the 100 cases a Wassermann examination of the blood was made; all were negative. In 36 cases the spinal fluid was examined; of these there were 32 negative and 4 positive Wassermann reactions (two of these were negative on later examination). The cell count was under 5 per cubic millimeter in 29 cases, and increased in 7 (from 10 to 90 cells). The globulin content was normal in 29 and increased in 7 cases. The colloidal gold curve was negative in 32 cases. In 4 cases it was as follows: 0034555310, 3532111000, 2222222222, and 1111110000. The tumor was not of syphilitic origin in any of the cases of this series. The occasional occurrence of a gumma of the brain cannot be disputed. It is unfortunate that the medical profession is under the impression that such a lesion is of frequent occurrence. Many of the 100 patients had received prolonged antisyphilitic treatment before being referred to the neurologic surgeon. Such a practice cannot be too strongly condemned.

Duration of Symptoms Before Diagnosis.—As evidence of the necessity of a continued effort on the part of the neurologist to teach the general physician the signs and symptoms which should at least suggest the possibility of intracranial neoplasms, we wish to submit the following rather startling facts:

The average duration of symptoms before a correct diagnosis was made in tumors of different locations is listed in table 5. The symptoms in one case of tumor of the frontal lobe had been present fourteen years before the diagnosis was made. These symptoms, for many years, were convulsions of a generalized character. The earliest case diagnosed after the development of symptoms was a tumor of the temporal lobe. In this case, symptoms had been present for only ten days. The next earliest was a cerebellar tumor in which the symptoms had been present only three weeks. The average duration of symptoms in all 100 cases before the diagnosis was made was twenty-seven months. It would seem that many of these cases should have been diagnosed earlier. It is unquestionably true that many tumors of the brain exist for a considerable time before the development of symptoms. A recent case (not included in this series) illustrates this point. A patient had motor aphasia and right sided weakness of three weeks' duration with no other symptoms. A large gliomatous cyst of the left frontal lobe was found

at operation. Such a condition had evidently existed for many months before the development of symptoms.

Table 6 illustrates the duration of symptoms before diagnosis in the different types of tumors.

TABLE 5.—*Duration of Symptoms Before Diagnosis in Tumors of Various Locations*

Location	Number of Cases	Average Duration of Symptoms Before Diagnosis
Frontal	10	36 months
Cribriform	2	11 months
Precentral	18	24 months
Postcentral	8	18 months
Temporal	11	16 months
Occipital	2	5½ months
Pituitary	10	55 months
Cerebellar	18	15 months
Angle	7	30 months
Pons	1	3 months
Falx	2	11 months
Pineal	2	15 months
Ventricle	1	4 months
Corpus callosum	2	84 months
Multiple	6	15 months

TABLE 6.—*Duration of Symptoms Before Diagnosis in Various Types of Tumors*

Type of Tumor	Number of Cases	Average Duration of Symptoms Before Diagnosis
Glioma	63	24 months
Endothelioma	11	11 months
Angioma	1	84 months
Perithelioma	4	11 months
Neurinoma	6	34 months
Tuberculoma	1	3 months
Melanoma	2	1½ months
Psammoma	1	4 months
Carcinoma	2	19 months
Adenoma (pituitary)	5	96 months
Chiasmal cyst	4	16 months

TABLE 7.—*Duration of Symptoms Before Diagnosis in Various Decades of Life*

Age of Patient	Number of Cases	Average Duration of Symptoms Before Diagnosis
Under 10 years	15	9 months
10 to 20 years	14	19 months
20 to 30 years	13	41 months
30 to 40 years	28	41 months
40 to 50 years	15	38 months
50 to 60 years	13	18 months
60 to 70 years	2	6 months

The duration of symptoms before the diagnosis was made in persons of various ages is placed in table 7. It is interesting that the diagnosis was made earlier after the development of symptoms in children under 10 years of age. In 9 of the 15 cases which occurred in children under 10 years of age the tumors were located below the tentorium. The early

development of the symptoms of increased intracranial pressure might easily explain the comparative promptness of the diagnosis.

First Symptom Noted.—It will be observed on referring to table 8 that the first symptom noted was indicative of increased intracranial pressure in 57 of the 100 cases. In the remaining 43 cases, the first symptom noted had a localizing significance. In those cases in which the first symptom noted was due to increased intracranial pressure, the

TABLE 8.—*First Symptom Noted*

Location	Number of Cases	First Symptom Indicating General Pressure	Symptoms of a Localizing Significance
Frontal	10	8 cases (80%) headaches or generalized convulsions	2 cases (20%); eccentric conduct, 1 case; numbness of right arm, 1 case
Cribriform	2	1 patient complained of bitemporal headaches	1 patient developed first a loss of interest in external things, social activities, etc.
Precentral	18	6 cases; 2 headaches and 4 generalized convulsions	12 cases (66.6%) as follows: local exostoses on skull, 1 case; numbness in contralateral extremity, 3 cases; jacksonian attacks followed by localized paralysis, 6 cases; localized paralysis without convulsions, 2 cases
Postcentral	8	3 cases (37%); generalized convulsions, 1 case; dizziness, 1 case; headache, 1 case	5 (63%); change of disposition (irritability), 1 case; localized attacks of numbness, 3 cases; awkward use of hand, 1 case
Temporal	11	8 (72%); headaches, 4 cases; diplopia, 1; generalized convulsions, 2; blurred vision, 1	3 (28%); weakness one side, 2; paresis right side of face, 1 case
Occipital	2	1 patient had headache first	1 case began with attacks of hemianopia
Cerebellar	18	17 (95%) began with headaches, vomiting, or pain in the neck	1 (5%) began with staggering gait
Angle	7	2 (28%) began with headache, vomiting, or pain in the neck	5 (72%); deafness, 3 cases; tinnitus, 1 case; numbness in face, 1 case
Pons	1	.....	The one case began with internal squint
Pineal	2	1 began with difficulty in focusing eyes	1 began with deafness
Falx	2	.....	Jacksonian attacks in 1 case; localized paralysis after generalized attack in 1 case
Corpus callosum	2	Convulsions in 1 case; headaches in 1 case	
Lateral ventricle	1	Shooting pains in head	
Pituitary	10	5 (50%); headaches, 4 cases; diplopia, 1 case	5 (50%); disturbed vision, 4 cases; obesity, polyuria, etc., 1 case
Multiple	6	2 (33%) headaches	4 (66.6%); localized numbness, 1 case; jacksonian attacks, 1 case; tinnitus (acoustic) 1 case; aphasia (auditory), 1 case

general symptoms were as follows: headaches 66 per cent, vomiting 4 per cent, convulsions 16 per cent, dizziness 5 per cent, visual disturbance 8 per cent, and mental changes 1 per cent.

Incidence of Tumors.—The incidence of the various types of tumors observed in the series conforms closely to the experience of those who have reported a much larger number of verified tumors. There were 63 gliomas, 11 endotheliomas, 10 chiasmal tumors, 6 acoustic neurinomas and 10 other rarer tumors. We have grouped the location and type of tumors in table 9.

It would seem from table 10 that practically no age is exempt from the usual tumors encountered. The one case of tuberculoma occurred in a child under 10 years of age. Endothelioma was not encountered in the first decade of life, nor was an adenoma of the chiasmal region

TABLE 9.—*Location and Type of Tumor*

Location	Glioma	Endothelioma	Angioma	Melanoma	Perithelioma	Neurinoma	Tuberculoma	Psammoma	Carcinoma	Adenoma	Chiasmal Cyst	Total
Frontal	7	2	..	..	1	..	..	..	..	..	..	10
Cribriform	..	2	..	..	..	..	..	..	..	..	..	2
Precentral	14	3	1	..	..	..	..	..	..	..	..	18
Postcentral	7	..	..	1	..	..	..	..	..	..	..	8
Temporal	9	1	..	1	..	..	..	..	..	..	..	11
Occipital	2	..	..	..	..	..	..	..	..	..	..	2
Cerebellar	16	..	..	..	1	..	1	..	..	..	..	18
Angle	2	..	..	..	..	5	..	..	..	..	..	7
Pons	1	..	..	..	..	..	..	..	..	..	..	1
Pineal	2	..	..	..	..	..	..	..	..	..	..	2
Corpus callosum	2	..	..	..	..	..	..	..	..	..	..	2
Falx	..	2	..	..	..	..	..	..	..	..	..	2
Lateral ventricle	..	..	..	..	..	..	..	1	..	..	..	1
Pituitary	..	..	..	..	..	..	..	..	1	5	4	10
Multiple	1	1	..	..	2	1	..	..	1	..	..	6
Total	63	11	1	2	4	6	1	1	2	5	4	100

TABLE 10.—*Type of Tumor Occurring in Different Decades*

Age of Patient	Glioma	Endothelioma	Angioma	Melanoma	Perithelioma	Neurinoma	Tuberculoma	Psammoma	Carcinoma	Adenoma	Chiasmal Cyst	Total
Under 10 years	11	..	..	..	1	1	1	..	..	..	1	15
10 to 20 years	12	1	1	..	..	..	..	..	..	..	..	14
20 to 30 years	5	3	..	..	..	1	..	..	1	1	2	13
30 to 40 years	18	3	..	1	2	1	..	..	1	2	..	28
40 to 50 years	9	1	..	..	..	2	..	1	..	1	1	15
50 to 60 years	6	3	..	1	1	1	..	..	..	1	..	13
60 to 70 years	2	..	..	..	..	..	..	..	..	..	..	2
Total	63	11	1	2	4	6	1	1	2	5	4	100

seen in the first two decades. No conclusions, however, could be drawn from such a small series of tumors.

The location of the tumors occurring in the various decades of life can be seen in table 11. It is an interesting fact that 13 of the 18 tumors of the cerebellum occurred during the first decades of life, and 8 of the 10 tumors of the frontal lobe occurred between 30 and 60 years of age.

It has been an accepted fact that intracranial tumors are more prevalent in males than in females. Our statistics show this to be true (table 12). Sixty-three of the cases occurred in males and 37 in females.

The types of tumor occurring in both sexes are listed in table 13

TABLE 11.—*Location of Tumor Occurring at Different Ages*

Location	Under 10 Years	10 to 20 Years	20 to 30 Years	30 to 40 Years	40 to 50 Years	50 to 60 Years	60 to 70 Years	Total
Frontal	1	..	1	2	3	3	..	10
Cribriform	..	..	..	1	1	..	..	2
Precentral	2	4	..	6	2	3	1	18
Postcentral	2	..	..	3	1	1	1	8
Temporal	..	2	2	3	2	2	..	11
Occipital	..	1	..	1	..	..	..	2
Cerebellar	7	6	2	3	..	..	..	18
Angle	1	..	..	2	2	2	..	7
Pons	1	..	..	..	..	..	..	1
Pineal	..	..	..	1	1	..	..	2
Corpus callosum	..	..	1	1	..	..	..	2
Falx	..	..	1	..	..	1	..	2
Lateral ventricle	..	..	..	..	1	..	..	1
Pituitary	1	..	4	2	2	1	..	10
Multiple	..	1	2	3	..	..	..	6
Total	15	14	13	28	15	13	2	100

TABLE 12.—*Location of Tumor in Different Sexes*

Location	Male	Female	Total
Frontal	6	4	10
Cribriform	1	1	2
Precentral	10	8	18
Postcentral	6	2	8
Temporal	8	3	11
Occipital	2	0	2
Cerebellar	9	9	18
Multiple	5	1	6
Ventricle	1	0	1
Pituitary	5	5	10
Pineal	1	1	2
Angle	5	2	7
Falx	2	0	2
Pons	0	1	1
Corpus callosum	2	0	2
Total	63	37	100

DIAGNOSIS

In the 100 cases a correct localizing diagnosis was made by routine neurologic examination in 75 cases, and by neurologic examination together with ventricular air studies in 14 other cases. A correct preoperative localizing diagnosis was thus made in 89 of the cases. In 11 cases, a correct preoperative localizing diagnosis was not made. In these cases the tumors were located as follows: 1 cribriform, diagnosed as a frontal tumor; 1 precentral, diagnosed as a cerebellar tumor; 3 temporal, 1 diagnosed as a cerebellopontile angle, 1 as a chiasmal, and 1 as an occiptal; 1 cerebellar, in which a tumor was not thought to

exist; 1 pineal, diagnosed as a cerebellar tumor; 1 cerebellopontile angle tumor, diagnosed as cerebellar (there was no deafness); 1 corpus callosum, diagnosed as a tumor of the parietal lobe; 1 multiple, diagnosed as a frontal abscess (this patient had a pituitary adenocarcinoma with metastasis to the cerebellum and left optic nerve); 1 multiple dural endothelioma, diagnosed as a tumor of the temporal lobe. It is interesting to note among the 4 remaining cases of multiple tumors, that the 2 tumors present were correctly localized in 1 case as the second tumor produced symptoms only after removal of the first (case 19). In the other 3 cases of multiple tumor, a correct localization of 1 of the tumors was made in each case.

The diagnosis was particularly difficult in 3 cases which were suspected as being vascular lesions. One of these was a tumor of the frontal lobe and the other two were tumors of the temporal lobe. The ages of these patients were 57, 48 and 59 years, respectively. In the two

TABLE 13.—*Type of Tumor Observed in the Two Sexes*

Type of Tumor	Male	Female	Total
Glioma	38	25	63
Endothelioma	7	4	11
Perithelioma	2	2	4
Adenoma	3	2	5
Chiasmal cyst	1	3	4
Psammoma	1	0	1
Neurinoma	5	1	6
Tuberculoma	1	0	1
Melanoma	2	0	2
Angioma	1	0	1
Carcinoma	2	0	2
Total	63	37	100

cases in which there were tumors of the temporal lobe a progressive hemiplegia suggesting an internal capsular lesion had occurred over a period of a few days. In the case in which the tumor of the frontal lobe occurred there was a weakness and numbness on one side and a systolic blood pressure of 195 mm. of mercury; there was a trace of albumin in the urine; renal function was 42 per cent and the nonprotein nitrogen of the blood was 27.2 mg. per hundred cubic centimeters; the spinal fluid contained 40 cells per cubic millimeter, and a trace of globulin; there was mild bilateral choking of the optic disks. Five cases began with fever suggesting encephalitis. There was a history of injury to the head in only 9 cases (2 endotheliomas, 4 gliomas, 2 acoustic neurinomas, and 1 pituitary adenoma).

OPERATIONS

One hundred and forty-two operations were performed in this series of 100 cases. With the exception of a few cases a radical approach was made in order to expose the tumor, with an attempt at removal of

the growth if the lesion disclosed seemed to justify such a procedure. In a few cases of patients in extremis a simple subtemporal decompression was performed as a palliative measure in the hope that the patient's condition would later improve sufficiently to permit a more radical procedure. In one case of a very large endothelioma originating from the falx, four unsuccessful attempts were made to expose the tumor, the operations having to be abandoned on account of excessive hemorrhage. In several other cases the operation had to be performed in two stages.

TABLE 14.—*Operation (Location of Tumor)*

Location	Number of Cases	Number of Operations
Frontal	10	14
Cribriform	2	2
Precentral	18	26
Postcentral	8	8
Falx	2	5
Multiple	6	7
Temporal	11	14
Occipital	2	3
Angle	7	12
Pineal	2	3
Cerebellar	18	26
Corpus callosum	2	3
Pons	1	1
Ventricle	1	4
Pituitary	10	14
Total	100	142

TABLE 15.—*Operations (Type of Tumor)*

Type of Tumor	Number of Cases	Number of Operations
Glioma	63	85
Endothelioma	11	19
Perithelioma	4	4
Angioma	1	1
Melanoma	2	2
Tuberculoma	1	2
Adenoma	5	16
Neurinoma	6	9
Chiasmal cyst	4	8
Carcinoma	2	2
Psammoma	1	4
Total	100	142

Whenever the lesion could not be removed, a liberal decompression was done, and the patients were given roentgen-ray treatments. In tables 14 and 15 are given the number of operations performed according to location and type. There were five cases in which operations were not performed.

LENGTH OF LIFE

The duration of life in patients having a tumor of the brain depends on several factors: the location of the tumor, the rapidity of the growth, early diagnosis, accuracy of the localizing diagnosis and the therapeutic measures used. It is also true that the length of life depends on the

degree of malignancy of the tumor. This varies especially in the glioma group. We have observed that the duration of life is much longer in those gliomas composed of cells of a mature type (astrocytoma) than when the cells are of a less differentiated character (spongioblastoma). Consequently, the duration of life is an individual matter and we do not believe any general statement or figures can be given for the prognosis of tumor of the brain in general.

In the 100 cases, operations were not performed in five and death occurred before operative consent could be obtained or before operation could be performed. In 4 of these cases, death occurred three months after the onset of symptoms; the tumors were a parietal glioma, a temporal glioma, a temporal melanoma and a cerebellar ependymoma. The fifth case, a pituitary adenoma, had given symptoms due to endocrine dysfunction for ten years. Of the remaining 95 patients, 24 are now living. The tumors in the cases of these living patients were located

TABLE 16.—*Length of Life (with Type and Location of Tumor) to Date*

Location.	Type	Duration Since Operation	Duration Since First Symptom
Frontal	Glioma	19 months	10 years
Precentral	Glioma	30 months	42 months
Falx	Endothelioma	66 months	90 months
Postcentral	Glioma	24 months	30 months
Temporal	Glioma	44 months	68 months
Lateral ventricle	Psammoma	9 months	14 months
Angle	Neurinoma	6 months	42 months
Pineal	Glioma	12 months	11 years
Pituitary	Adenoma	24 months	48 months
Cerebellar	Glioma	5½ years	8½ years
Cerebellar	Glioma	4 years	8 years
Cerebellar	Glioma	3 years	4 years

as follows: frontal 3, falx 1, precentral 4, postcentral 2, temporal 2, cerebellum 7, chiasmal 2, angle 1, pineal 1 and lateral ventricle 1. The types of tumors encountered in the twenty-four living patients were: glioma, 15; endothelioma, 3; perithelioma, 2; angioma, 1; psammoma, 1; pituitary adenoma, 1 and pituitary cyst, 1. There was one patient under 10 years of age, five between 10 and 20, three between 20 and 30, nine between 30 and 40, four between 40 and 50 and two between 50 and 60 years of age.

The length of life in the living patients varies considerably among the patients with the tumors of any particular location or type. Some examples from this group are given in table 16.

We believe that the examples cited should emphasize the necessity for diligence in the early recognition and treatment of tumor of the brain, concerning which there has been too much pessimism.

Seventy-one patients died at some time after operation; of these, twenty-six died within the first twenty-four hours. It may appear that this is a high operative mortality. Many of these patients were mori-

bund when first seen, and were operated on with the realization that the chances for recovery were small. It has already been stated that an average of 27.5 months elapsed between the onset of symptoms and the time of diagnosis. From this it can readily be seen that the disease was often far advanced before coming to operation. Should the time come when tumors of the brain are diagnosed soon after the onset of symptoms it is not too much to expect that more patients should be cured, and the operative mortality lessened. The operative deaths occurred in tumors of the following locations: 3 frontal, 1 cribriform, 2 precentral, 1 postcentral, 4 temporal, 2 cerebellar, 3 pituitary, 1 pons, 4 angle, 1 pineal and 4 multiple tumors.

The patient with tuberculoma of the cerebellum died of tuberculous peritonitis four months after operation, and six months after the onset of symptoms. Some other examples of the patients now dead are given in table 17.

TABLE 17.—*Relation of Duration of Symptoms to Death*

Location	Type	Time of Operation Before Death	Duration of Symptoms Before Death
Frontal	Perithelioma	9 months	10 months
Cribriform	Endothelioma	3 months	9 months
Precentral	Glioma	28 months	9 years
Postcentral	Glioma	19 months	48 months
Temporal	Glioma	11 months	36 months
Occipital	Glioma	10 months	17 months
Angle	Neurinoma	11 months	7 years
Cerebellum	Glioma	13 months	42 months
Chiasm	Cyst	7 years	14 years
Corpus callosum	Glioma	1 week	6 years

The average duration of life of those now dead (exclusive of the nonoperative cases and the patients dying within twenty-four hours after operation) was 41.2 months after the development of symptoms.

CONCLUSIONS

In a review of 100 consecutive verified intracranial tumors, the following features of interest were observed:

1. Headache occurred in 81 per cent. In the cases of cerebellar tumor in which headache was once complained of, it never ceased until after operation. The type of headache noted in the series varied from a dull steady ache to severe intermittent pains of neuralgic character. The location of the headache bore no relation to the site of the tumor. This symptom was the first noted in 37 per cent of all cases.

2. Vomiting was present in 54 per cent. In only 11 per cent was it projectile. It was the initial symptom in 2 per cent.

3. Visual disturbances were complained of in 53 per cent. The ocular fundi were normal in 14 per cent. Papilledema was present in

66 per cent. Optic atrophy without choking was noted in 14 per cent. Studies of the visual field were of definite localizing value in 16 per cent. Complex visual hallucinations were present in only one case of tumor of the temporal lobe. Diplopia due to paralysis of the sixth cranial nerve was of localizing value in only one case (tumor of the pons).

4. Convulsive seizures were present in 39 per cent. In 54 per cent of these the convulsions presented features of localizing value. Tonic seizures were present in two cases (subtentorial tumors).

5. Mental disturbances were present in 31 per cent; the earlier the development of these symptoms the more anterior was the tumor located.

6. Vertigo was complained of in 29 per cent and was of no localizing value.

7. Anosmia was present in 10 per cent. This observation was most important in the diagnosis of tumors overlying the cribriform plate.

8. Increase in blood pressure or slowing of the pulse rate was noted only in the terminal stages of medullary compression.

9. Roentgen-ray studies of the skull revealed abnormalities of localizing value in 21 per cent of the cases. Ventriculograms were of essential value for localization in 14 per cent.

10. Studies of the spinal fluid were of no significance as far as diagnosis was concerned. There were four cases in which the Wassermann reaction of the spinal fluid was positive; in none of these was a gumma of the brain present.

11. The average duration of symptoms before diagnosis was 27.5 months.

12. The first symptom indicated increased intracranial pressure in 57 per cent and a focal lesion in 43 per cent. When the first symptom was of localizing value the tumors were located chiefly in the rolandic region and in the cerebellopontile angle.

13. Thirteen of the 18 cerebellar tumors occurred in patients under 20 years of age. Eight of the 10 tumors of the frontal lobe occurred after the patients were 30 years of age.

14. There were 63 gliomas, 11 endotheliomas, 10 chiasmal tumors, 6 acoustic neurinomas and 10 other rarer tumors.

15. A localizing diagnosis on neurologic examination was made in 75 per cent, and with the aid of ventriculograms in 89 per cent.

16. Duration of life in cases of tumor of the brain cannot be stated in general terms but depends on the location and type of the tumor. Of the 100 patients 24 are now living.

THE HYPERPNEA TEST IN EPILEPSY *

JOSEPH FETTERMAN, M.D.
CLEVELAND

Hyperpnea has proved of value in throwing light on the mechanism of epilepsy and in the differential diagnosis of various forms of this disorder.

The first mention of muscle spasms during hyperpnea is credited to Vernon [1] who was experimenting with "apnea." He observed "my hands got into a state of tonic rigidity and were then paralyzed after breathing deeply a long time." Later, Rosett [2] published an article entitled "The Experimental Production of Rigidity in Man," and in this report he went thoroughly into the technic, results and interpretations. Foerster,[3] of Breslau, emphasized the value of this procedure in cases of traumatic epilepsy. He found that increased muscle irritability was induced by the overventilation. Heidrich [4] has confirmed this work and cites two cases in which hyperpnea helped to establish the diagnosis of a lesion of the brain. Guillain and others [5] commented on the usefulness of voluntary hyperpnea in jacksonian epilepsy.

Muck [6] tried the hyperpnea procedure in cases in which migraine was suspected and found that by the deep breathing method he could induce a sensation of "headache, spots before the eyes, and chilliness," akin to actual migraine, whereas his normal controls did not show any such response. Lange and Gutman [7] have attempted to explain a case of hystero-epilepsy by this mechanism. They reported the instance of a young woman, who, during an hysterical outburst, breathed so deeply

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* From the Neuropsychiatric Dispensary, at Lakeside Hospital, Cleveland. This study was done under the direction of Dr. C. W. Stone, chief of the Neuropsychiatric Clinic.

1. Vernon, H. M.: The Production of Prolonged Apnea in Man, J. Physiol., 1909, vol. 38.

2. Rosett, J.: The Experimental Production of Rigidity in Man, Brain **47**:292, 1924.

3. Foerster, quoted by O. Muck: München. med. Wchnschr. **73**:982 (June) 1926.

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5. Guillain et al.: Voluntary Hypernea Test Applied to Jacksonsian Epilepsy, Bull. et. mém. Soc. méd. d. hôp., Paris; abstr., J. A. M. A. **84**:1457 (May 9) 1925.

6. Muck, O.: Hyperventilation Migraine, München. med. Wchnschr. **73**: 982 (June) 1926.

7. Lange, J., and Gutman: Hysterical Attack and Hyperventilation, München. med. Wchnschr. **73**:983 (June) 1926.

in and out that she threw herself into what appeared to be a true epileptic convulsion.

On the other hand, there have been reports in the literature of failures to induce significant muscle and mental changes by this procedure. Janota [8] did not find any changes in electrical excitability, and only one of his patients developed a seizure. It is only fair to state that Focher [9] has expressed the opinion that methods provocative of an attack are harmful—yet I have seen discomfort attributable to hyperpnea in only one of seventy such tests. One of my patients, a young woman with idiopathic epilepsy whose attacks were infrequent, had a seizure on the day following the test; she accused the excessive ventilation and muscular effort as being the cause.

EXPERIMENTAL WORK

Technic Employed.—Following Rosett's directions, I tried the hyperpnea test on a number of my patients. I place the patient, partially or totally stripped, on a table and instruct him to inhale and exhale deeply at the rate of about twelve times a minute. Careful attention is paid to see that the respiratory movements are as complete as possible. Over seventy-five such tests have been made on thirty-five epileptic patients and three controls.

The Occurrences in the Course of Deep Breathing.—In the average case, after the deep breathing is instituted for a few minutes, the patient appears drowsy and yawns. His color becomes more pink than usual, his eyes shiny, and the pupils dilate somewhat. After an additional five minutes, he complains of being dizzy or tired. By this time (in some cases much earlier and in others later) various muscle quiverings are visible in the face, neck or chest. Sometimes there are spasms of the fingers and occasionally generalized convulsions (fig. 1). In negative cases, however, the breathing is continued for from a half hour to an hour and little if any change follows except drowsiness, fatigue and coldness in the fingers.

Strongly Positive Results.—In four of the thirty-five patients the test reproduced the attacks which the patient ordinarily had. In two of them the hyperpnea aided in the diagnosis and localization of a brain lesion.

CASE 1.—J. K., a man, aged 58, for ten years had had spasms and a feeling of coldness in the right hand. He showed facial paresis on the right. During

8. Janota: Provocation of Seizure, Čas. lék. česk. **64**:1717, 1925; abstr., J. A. M. A. **86**:238 (Jan. 16) 1926.

9. Focher, L.: A Diagnostic Symptom of Idiopathic Epilepsy, J. Nerv. & Ment. Dis. **42**:337 (Oct.) 1925.

the ten-year period he had only two generalized convulsions. The Wassermann tests on blood and spinal fluid were negative. A roentgenogram of the skull was normal.

The hyperpnea tests were repeated several times and in each instance induced a feeling of coldness in the finger tips, then extensor spasm of the fingers and twitchings of the right facial muscles; during this time breathing stopped and the patient appeared dazed.

This observation led to ventriculographic study which (Prof. E. C. Cutler and Dr. C. Beck) showed a deformed ventricle in the left cerebral hemisphere.

At a subsequent operation a large infiltrating glioma involving the left motor cortex was found and removed (as far as possible).

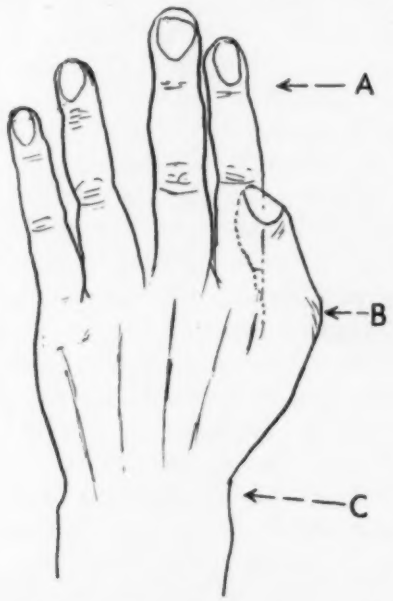

Fig. 1.—Hyperpnea hand. *A* indicates extension and spasticity of the fingers; *B* flexion and apposition of the thumb, and *C* extension of the wrist.

In this instance, the hyperpnea test led to a diagnosis of tumor of the brain.

Case 2.—Wm. K., a man, aged 35, about ten years before admission had been struck on the head. In a few months he developed spasms of the left side of the face and neck. These had continued with increasing severity up to the present, when he was having attacks almost every day.

During the hyperpnea procedure, after about five minutes of deep breathing the patient complained of feeling dizzy. Later, the left facial muscles twitched and the platysma quivered. Then the breathing stopped, the tongue was pulled sharply over to the left side and the muscles of the left side of the mouth and neck contracted forcibly. In a few minutes all was well again. When the deep breathing was reinstituted, there was a spasm of the upper eyelid, the left cheek muscle twitched and the tongue and neck muscles contracted.

The patient was referred to the surgical service with a diagnosis of an organic lesion. Prof. Cutler found pigmentation over the right motor cortex with a hemorrhagic cyst in the fissure of Sylvius, and scar changes in the brain substance. The cyst was removed. It is now about six months since the operation, and the patient has had no further spasms.

CASE 3.—J. M., suffering from epilepsy of long standing, probably of traumatic origin, was having about one attack (a generalized convulsion) per month.

The hyperpnea test began at 9:30. At 9:40 breathing ceased and the face assumed a masked expression. The teeth crunched, both arms lifted up in a spastic, rigid way. The fingers kept moving in circles for about two minutes. Then the patient got up, walked about the room in a daze and failed to respond to questions. Blankly, he made up a cigaret and when matches were offered he lighted it. Five minutes later he was able to answer questions.

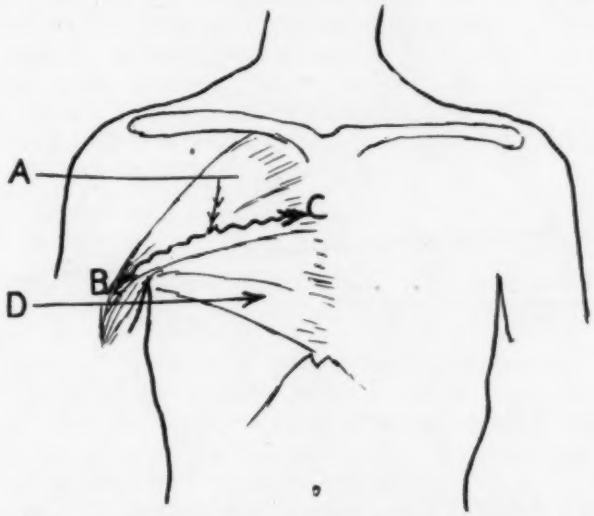

Fig. 2.—Diagram showing "muscle ripple." *A* indicates the point struck by reflex hammer. A hill of quivering muscle fiber forms. *B* and *C* show two fine waves running simultaneously in opposite directions like a section of a ripple. *D* is a diagrammatic sketch of the right pectoral muscle.

CASE 4.—G. B., a woman, with idiopathic epilepsy, was given a first hyperpnea test at a time when the convulsions were more frequent. After two minutes the breathing stopped, the face looked blank, the mouth twisted up to the right, and the eyelids closed and opened rapidly. The arms and legs stiffened and the patient cried out for her mother; a minute later she complained of stomach ache. Several minutes later she became clear.

Milder Changes Both Mental and Muscular.—In the following cases mild changes, both mental and muscular, were noted after the hyperpnea test:

CASE 5.—R. M., suffering from idiopathic epilepsy, had had frequent muscular tremors and occasional grand mal attacks. During the hyperpnea test there

was quivering of the eyelids, pulling over of the head to the side and spasm of the muscles of the arms.

Case 6.—H. O., suffering from idiopathic epilepsy, after about ten minutes of deep breathing developed a vague expression, as if in a trance, and there were quiverings of the muscles of the upper arms.

Case 7.—S. D., with epilepsy on an encephalitic basis, after ten minutes of deep breathing developed tremors of the left pectoral muscles with contraction of the extensor muscles of the hand. After about ten minutes he complained of a sensation as if "going to have another attack"; there were twitchings of the muscles of the face, and the fingers of the right hand assumed the position of the obstetrical hand.

Case 8.—W. Mc., with idiopathic epilepsy, after ten minutes of deep breathing developed a rise and fall of the left arm with each respiration; the fingers of the left hand were outstretched as in tetany.

Case 9.—M. S., with idopathic epilepsy, after ten minutes of deep breathing showed apnea and spasm of the fingers; later, there developed an obstetrical hand and then catatonia for a brief period.

Case 10.—R. W., with idiopathic epilepsy, after a few minutes of deep breathing showed shaking of the left arm and spasm of the left pectoral muscle.

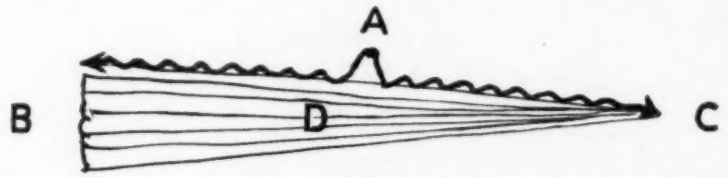

Fig. 3.—Diagram of "muscle ripple." *A* indicates the point struck; the swelling forms momentarily. *B* and *C* show the muscle origin and insertion toward which the fine waves travel; D, the muscle fibers.

She complained of feeling chilly and as if she were going to have an attack. The test was stopped.

Case 11.—W. D., an imbecile with idiopathic epilepsy, after about ten minutes of deep breathing showed apnea, twitchings of the muscles of the left side of the leg and left pectoral muscles, and slight dulness from which she was easily aroused.

Case 12.—M. D., a "feebleminded" epileptic, showed apnea after five minutes of deep breathing. Later, tremors of muscles about the right shoulder and arm and fine quivering of the platysma and facial muscles of the right side developed. Then there occurred spasm of the shoulder and elbow; later, the left arm was spastic. Constricting the arm with a blood pressure cuff did not check the spasticity or tremors.

Case 13.—Paul C., with idiopathic epilepsy, with deep breathing showed first opening and shutting of the eyelids. After fifteen minutes there was a vacant stare and he failed to respond to commands. Breathing became irregular. After forty-five minutes breathing stopped; the arms became catatonic, and the patient gazed vacantly into space. He did not answer questions and did not respond to commands for five minutes. Later he recovered.

Case 14.—A. M., with idiopathic epilepsy, had had convulsions on the same day. After ten minutes of deep breathing the features became flushed; fifteen

minutes later the right arm became spastic, the head was pulled over to the side, the gaze was blank and there was slight catatonia.

CASE 15.—A. K., with idiopathic epilepsy, after five minutes of deep breathing complained of feeling dizzy, had fibrillary twitchings and shaking of the head; later there were tremors of the face and the sternocleidomastoids contracted spasmodically.

CASE 16.—S. P., with organic epilepsy, after ten minutes of deep breathing developed twitchings of the facial muscles.

CASE 17.—R. B., with questionable idiopathic epilepsy developed quivering of the muscles of the chest; later, spasm of the jaws and quivering of the platysma; the eyelids closed and there was a spasm of the extensor muscles of the forearm on both sides.

CASE 18.—J. K., under the test showed jerkings of the head to the left, and of the platysma and the face muscles of both sides.

CASE 19.—M. M., when tested showed after ten minutes a short period of apnea, then fibrillary twitchings of the facial muscles with every inspiration. The hand assumed the obstetrical position and there was catatonia.

Mild or No Changes.—In a number of cases, mild or no changes were observed following the hyperpnea test.

CASE 20.—A. P., a feebleminded epileptic child, when tested showed slight twitching of the hand and slight tremors of the fingers.

CASE 21.—J. C., who had had idiopathic epilepsy but had been free from convulsions for one year, under test became after twenty-five minutes drowsy and yawned. There were no muscle changes.

CASE 22.—H. O., with idiopathic epilepsy, under test developed a stare like that in the petit mal attacks she used to have.

CASE 23.—A. S., with idiopathic epilepsy, under test developed sleepiness after ten minutes and complained of being tired. After thirty minutes there were no muscle tremors.

CASE 24.—M. S., with idiopathic epilepsy, under test after fifteen minutes became "dopey," and had a glassy stare. After thirty-five minutes, there were no muscle changes.

CASE 25.—A. B., with idiopathic epilepsy, under test after five minutes yawned; after twenty-five minutes complained of being dizzy. There were no muscle changes.

CASE 26.—W. M. had had frequent attacks of idiopathic epilepsy. Under test there were no changes after twenty minutes. Cooperation was poor.

CASE 27.—F. N., with idiopathic epilepsy, under test the eyes became shiny and there were slight tremors of the eyes and eyelids. The hands felt tired but there were no muscular changes.

CASE 28.—A. B., in whom there was a question of brain injury, after five minutes of deep breathing the eyeballs turned down. There were no other muscular phenomena.

CASE 29.—M. H., with probable hystero-epilepsy, under test showed slight quivering about the lips. The head felt funny; there were no muscular twitchings.

Case 30.—Hyman G., with idiopathic epilepsy, showed under test slight twitching of the eyelids. His seizures had been very infrequent.

Case 31.—L. D., with idiopathic epilepsy, on test showed slight twitching of the eyelids.

Case 32.—J. M., with idiopathic epilepsy, on test showed no changes whatever.

Case 33.—J. B., with idiopathic epilepsy, on test showed after fifteen minutes a vacant stare. There were no other changes.

Case 34.—B. K., a subnormal epileptic, on test showed no mental and no muscular changes.

Case 35.—E. K., an epileptic who had been receiving phenobarbital for several years, on test showed no changes.

Control Cases.—The hyperpnea test was given in a number of control cases.

Case 36.—M. K., suffering from a neurosis, under test showed slight spasm of the left hand; breathing was irregular. After thirty minutes, muscular changes were not noted.

Case 37.—X. Y., a neurotic person, under test complained of coldness of the hand and slight stiffness in the hand, but no muscular or mental changes were noted.

Case 38.—Y. Z., a healthy adult, under test complained of coldness in the hands, but no muscular or mental changes were noted.

Comment.—It has been my experience that children do not show such striking results as adults. This difference is due chiefly to the lack of cooperation in breathing.

It can be observed from the case reports that patients vary considerably in the muscular and mental changes induced by the hyperpnea procedure.

I noted also variations in the same person at different times, especially if the drugs administered were altered. To test this I repeated the experiment on the same subject after changing his medication. I found consistently, as did Rosett, that the previous use of phenobarbital protected against a convulsion; also that the use of potassium citrate rendered the patient more liable to the rigidity phenomena.

J. M., when receiving phenobarbital showed practically no changes; when given alkalis (potassium citrate) he developed the state of catatonia already referred to.

P. C., when taking phenobarbital became sleepy only after twenty minutes. When given ammonium chloride he showed physical and mental changes after long breathing. With administration of potassium citrate he again had twitchings and mental stupor.

Most of the patients who reacted only slightly to this experiment had been receiving phenobarbital or bromides for a considerable time before the test.

THE MECHANISM OF ACTION OF HYPERPNEA

Rosett attributed the muscular spasm to a hydrogen-ion change in the direction of alkalosis. He believed that the alkalosis caused dulling of the cerebral functions, especially if these were already affected. As the cortex and the spinal centers have reciprocal action, the cutting off of the mental control releases the muscular movements.

I have made few laboratory tests, but I did determine the carbon dioxide combining power of the blood before and after this test on several occasions and found no marked changes. In two cases, the results were as follows: In M. S., before hyperventilation, the carbon dioxide combining power was 61 per cent by volume; after hyperventilation it was 54; in A. P., the carbon dioxide combining power was 61 per cent by volume before hyperventilation, and 50 per cent by volume afterward.

In only two patients, or 86 per cent, did the carbon dioxide combining power after the hyperpnea test show a tendency toward alkalosis.

In contrast to the view of Rosett is the statement of Frisch and Fried,[10] who gave a table of the blood changes before and after hyperventilation and did not find a direct connection between alkalosis and convulsions. In five patients the figures were: p_H before hyperventilation, 7.5; 7.59; 7.52; 7.57; 7.51; and the p_H after hyperventilation, 7.75; 7.75; 7.64; 7.74; 7.64.

When, in these patients, the p_H was changed from 7.5 to an alkalosis a convulsion did not necessarily take place. At times, also, there were convulsions in the absence of alkalosis. Dr. F. Mainzer[11] expressed the opinion that a change takes place in the colloid-chloride state which is instrumental in causing the convulsion.

It occurred to me that perhaps the sudden and frequent changes of the pressure in the brain might account for the symptoms. I have noticed occasionally that striking results took place after only a few minutes and that the symptoms did not depend on the duration of the hyperpnea.

THE MUSCLE RIPPLE

Several German authors have observed a change in the electric excitability resulting from hyperpnea. I regret that I did not make such tests.

In the course of my experiments, however, I happened to strike the pectoral muscles rather vigorously during the course of hyperpnea and was surprised to see the following phenomenon: A small elevation

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10. Frisch and Fried: Zur Frage der angeblichen Alkalose, Ztschr. f. d. ges. exper. Med. **49**:462, 1926.

11. Mainzer, F.: The Chemistry of Induction of Epileptic Attacks by Hyperventilation, Klin. Wchnschr. **4**:1918 (Oct. 1) 1925.

of the muscle would take place at the point struck, and then two waves would travel in opposite directions from this point toward the ends of the muscle. These waves traveled for a distance of from 2 to 4 inches (5 to 10.16 cm.) The swelling would disappear and occasionally a second wave would start. This phenomenon resembles so much the wave or ripple in water when a stone is dropped that I have used the expression "muscle ripple." This phenomenon could be elicited best by tapping the pectoral muscle at about the nipple line. A ripple-like wave traveling in both directions would appear. The wave came distinctly later than the muscle fiber contraction and was independent of it. The ripple traveled always in a straight direction from the place struck toward the origin and insertion of the muscle (fig. 2).

I have found this phenomenon also occasionally in the back muscles. Strong striking of the biceps muscle at the center of its belly or sudden pinching produced a similar wave. I observed this in several epileptic patients and also found it in: (1) a patient who had had chronic anterior poliomyelitis; (2) a patient who had had a hemorrhage into the pons, and (3) a case of exophthalmic goiter. This fine ripple was observed only in males; apparently the adipose layer in women obscured it.

In connection with hyperpnea I found on many occasions that, although no ripple was present before the breathing began, it appeared and remained during the deep breathing. The muscle ripple is a sign of muscle irritability.

THERAPEUTIC APPLICATION

On the basis that hyperpnea is conducive to convulsions the thought occurred to me that apnea might protect against them. I therefore advised my epileptic patients to exhale to the maximum and to hold the breath, keeping the arms tense and all muscles of the thorax contracted. In the past six months several patients had occasion to test this procedure clinically with the appearance of a warning of an attack. Often the premonitory symptoms disappeared and the attack did not develop.

SUMMARY

The hyperpnea procedure is practically harmless and yet has value, particularly in organic cases. Here it can be of great value both in diagnosis and in localizing the lesion. The case reports show likewise that even in idiopathic cases significant changes may not take place. I have made clinical application of the fact that hyperpnea causes convulsions by employing apnea as a means for preventing them. I have observed a muscle phenomenon, "the muscle ripple," which appears to be a sign of increased irritability.

Abstracts from Current Literature

DIABETES INSIPIDUS. A CLINICAL REVIEW AND ANALYSIS OF NECROPSY REPORTS. E. B. FINK, Arch. Path. **6**:102 (July) 1928.

Diabetes insipidus is a clinical syndrome, the outstanding symptoms of which are polyuria and polydipsia. It is rare, being found in 0.01 per cent of all patients treated. The etiology is still obscure. Certain facts are well known: temporary polyuria occurs in hysteria and in severe emotional stress. It frequently follows severe injuries at the base of the skull. Syphilitic basal meningitis is at times a cause and has been emphasized by Oppenheim. It may occur during convalescence from any of the acute infectious diseases. It has been reported following epidemic encephalitis. It has been found in association with tumors at the base. The symptoms may occur slowly or suddenly, depending on the etiologic factor. As a rule the course is chronic. The classic symptoms are permanent polydipsia and polyuria, with the excretion of a sugar-free, watery urine. The amount of urine may vary from a slight increase above the normal to enormous quantities in twenty-four hours. The ordinary tests for renal function do not usually show deviations from the normal.

Complete agreement regarding the pathologic physiology of diabetes insipidus has not been reached. The pathologic lesions held responsible for this condition divide themselves into three distinct types, depending on prevailing theories and the experimental production of polyuria. The first was influenced by Claude Bernard's classic experiment in which he demonstrated that piqûre of the corpus restiforme in the floor of the fourth ventricle was followed by polyuria. The same result was obtained by Eckhard by means of injury to the pons and cerebellum. The second period may be termed the hypophyseal period, and it had its origin in a paper by Frank in which he directed attention to the frequent association of diabetes insipidus with signs of pituitary lesions. He emphasized the fact that the classic symptom of pressure arising in the hypophysis or its immediate vicinity is bitemporal hemianopia caused by pressure on the optic chiasm and stated that it was remarkable that two such rare symptoms as bitemporal hemianopia and polyuria should frequently occur together. The third period is based on experimental physiology and finds its origin in the work of Camus and Roussy, who showed that injury to the floor of the third ventricle near the insertion of the infundibulum leads to polyuria, although Aschner claimed priority in these experiments. Leschke was among the first to maintain that diabetes insipidus is due to a lesion at the base of the midbrain and based his arguments on a large amount of clinical material. As a result of the implication of the base of the brain in the genesis of diabetes insipidus, numerous histologic studies of this region have been made. An excellent summary of the structure and pathologic changes of the vegetative centers of the midbrain was given by Greving. That the centers in the tuber cinereum exert a regulatory influence on metabolism of water and salt has undoubtedly been proved by experimental physiologists. That these centers act independently of the hypophysis has certainly not been demonstrated. Evidence is constantly accumulating that the hypophysis and the diencephalic centers form an anatomic and probably also a functional unit. The relationship between the hypophysis and diencephalic centers was studied extensively by Espino, who found that comparative anatomy furnishes evidence of a close relationship between the hypophysis and diencephalon in the entire series of animals possessing a hypophysis. In man such a relationship exists between the tuber cinereum, infundibulum and hypophysis from early intra-uterine life.

Fink was able to collect from the literature records of 107 necropsies in cases of diabetes insipidus. These are given in three tables. Of these, 63 per

cent showed tumors about the base of the brain or posterior cranial fossa; 13 per cent were due to syphilitic processes, either basal meningitis or gummas in or near the pituitary; in five cases, the lesion was a tuberculoma or tuberculous meningitis of the base, and nine were due to nonsyphilitic inflammatory conditions in the same location. The remainder are included under traumatic injuries. The majority of the cases in which a tumor was present are not of localizing value since they have involved more than one structure in the narrow space at the base of the brain. There are fifteen instances of a discrete metastatic carcinoma nodule limited to the posterior lobe of the hypophysis or infundibulum. Ten cases are on record of a gumma or caseous tubercle in the same location. In a recent case reported by the author, he failed to find any pathologic change in the tuber cinereum.

In treatment, the first factor is, of course, the etiology. In syphilis, the treatment is evident. Spinal puncture in the other cases, first advocated by Herrick, has proved of little real value. The restriction of water accomplishes nothing, is an unnecessary cruelty and may even be dangerous. The most important contribution to the treatment was made by von den Velden, in 1913, when he demonstrated that in persons with normal kidneys the subcutaneous injection of pituitary extract produces a reduction in diuresis instead of an increase as had been previously indicated by physiologic experiments. The greatest objection to the use of pituitary extract is the need for repeated hypodermic injections. This may be overcome in cases in which it is effective by means of a spray, a medicine dropper or a tampon as suggested by Blumgart.

The author sums up his article as follows: Diabetes insipidus is a clinical syndrome without a uniform pathologic basis. A study of necropsy reports shows that there are cases on record which can be used in favor of any theory one may wish to favor. Experimental polyuria has been produced by lesions in the floor of the fourth ventricle, separation of the pituitary stalk and injury or stimulation of the tuber cinereum, the corpora quadrigemina, the pons and the cerebellum. Every part of the base of the brain has been implicated at one time or another.

In considering the pathologic changes in diabetes insipidus, those cases in which the lesion is confined to the posterior lobe and infundibulum cannot be ignored. When polyuria develops in a person with malignant disease, it is almost a pathognomonic sign of a metastasis in the posterior lobe of the hypophysis. The posterior lobe of the hypophysis is a part of the diencephalon, both genetically and anatomically. In the light of present knowledge, the hypophysis and the centers in the midbrain must be considered as a functionally united system. Injury to any part of this system may result in diabetes insipidus, although it does not invariably do so. The underlying factors that determine whether polyuria shall or shall not develop in a given case are not known.

The theory that harmonizes most closely with the facts is that the function of the kidney is under the influence of three factors: the kidney itself and its autonomic nerves; a vegetative center, probably located in the tuber cinereum, and a pituitary hormone. Injury to, failure of function of, or irritation in any of these controlling factors may result in the symptom-complex diabetes insipidus.

WINKELMAN, Philadelphia.

STUDIES IN REFLEXES IN AN ANENCEPHALIC MONSTER. ERNST TRÖMNER, J. f. Psychol. u. Neurol. **35**:194, 1928.

The monster was a female child, born after a nine and a half months' pregnancy; it weighed 7 pounds (3.2 Kg.) and was 53 cm. long. A history of syphilis, trauma or alcoholism in the parents was not obtained. It lived two days. The body was normal and well developed, especially the thorax and shoulders. It had a typical "frog's head," with unusually prominent eyeballs. The top of the skull was reduced to a narrow ring and was replaced by a dark red placental-like

mass, the substantia cerebrovasculosa (Cruveilier), which terminated in the frontal portion in two cysts that were filled with bloody serum. Viewed from the top, a rudiment of both cerebral hemispheres could still be seen.

The monster lay on its back with the head and face immobile, and the arms and lower limbs in flexion; occasionally, all extremities would spontaneously develop trembling movements which were neither choreiform nor athetoid. The lids were half closed, the eyes somewhat diverging and occasionally blinking, although the eyeballs remained absolutely immobile. The pupils were rigid and the cornea dry, and without reaction. Though unable to sit, the monster would grasp the examiner's finger inserted into its palm, so that its body would be raised almost 10 inches (25.4 cm.) above the reclining surface.

Response was not obtained to visual, auditory, olfactory or gustatory stimuli, although compression of the lips and mouth was followed by a slight hollowing out of the tip of the tongue and a few disordered movements of the lips; sucking and chewing movements, however, were not noted. Tactile and thermal (heat) stimuli did not elicit any response, but painful and extremely cold stimuli were followed by a few movements. Every painful stimulus (pinching or pricking) was followed by a shower of tremors. The application of ice to the back of the neck produced extension of the head backward; a shaking up of the body was followed by a sort of a Moro reflex (the body would pull itself together, and at the same time the lower limbs would be raised and the arms extended). Percussion of one side of the chest produced extension of the homolateral arm, but neither labyrinthine nor neck reflexes could be elicited.

Examinaton of the motility of the muscles revealed a somewhat normal muscle tonus; at any rate, decerebrate rigidity was not noted; all muscle reflexes (in the author's sense), except the masseter reflex, were retained. The reflex contractions were lively and definite, frequently even multimuscular, though never clonic. Some muscle reflexes obtained by the percussion of the muscle were also retained (reflexes of the abdominal muscles). All cutaneous reflexes were present: Stroking of the palm was followed by the making of a fist and pronation, stroking of the abdominal wall by a cutaneous abdominal reflex and stimulation of the sole by a lively plantar reflex with slight contraction of the tibialis posticus; Mayer's thumb reflex was not demonstrable.

Another interesting though not unusual feature was a congenital lesion of the heart. The body did not show any other evidences of malformation. This, however, is not surprising, because even in the more rare cases of amyelia the body and muscular system are usually well developed. As a matter of fact, Modenau and others have shown that not even a spinal cord is absolutely essential for the development of a normal well striated musculature.

The presence of normal muscle tonus in a spinal animal such as this monster seems to show that muscle tonus and muscle reflexes can be regulated by purely spinal mechanisms, and that extrapyramidal, i. e., striopallidal influences, are not at all necessary for these functions. The author, therefore, does not have any doubt that the extrapyramidal system can only have a hypertonic effect when it is in a state of irritation. Further discussion as to the genesis of the muscle reflexes must be postponed until the microscopic examination of the cord has been completed, even though R. A. Pfeiffer's and Cornil Bertillons' case (anencephalus developed up to the pyramidal decussation) permitted the conclusion that all muscle reflexes depend relatively on a purely spinal function, which in its earliest stages is independent of cerebral mechanisms.

The grasping reflex in this case is regarded by the author as analogous to the plantar reflex. The plantar reflex, as obtained in this case, he believes, is definite evidence that this form of reflex represents a primitive archaic form of a sole reflex, and that an extensor plantar reflex does not occur until the higher centers have come into activity.

Contrary to Head's conception, which also includes the sensation of warmth among the protopathic types of sensibility, observation of this anencephalic monster, responding only to cold stimuli (the application of ice to the back, followed by a movement of the head), would seem to show that pain and cold are most primitive

stimuli; these, by endangering the organic condition of the body are followed by responses much more readily than touch and warmth. Cold and pain, therefore, are purely spinal responses and may act as a Babinski-producing stimulus in transverse lesions of the cord, even though all conscious sensations have disappeared.

The paper is concluded with a discussion of the various theories advanced to account for the greater frequency of anencephalus in females than in males. Trömner rejects the hypotheses offered by gynecologists and endocrinologists as to the effects of a poorly developed endocrine anlage with consequent hormonal disturbances as pathogenetic factors, but he himself does not have a better theory than that "one must assume that cerebral morbidity is greater in female than in male fetuses."

KESCHNER, New York.

THE RELATIONSHIP OF CHRONIC SUBDURAL HEMATOMA AND PACHYMENINGITIS HEMORRHAGICA INTERNA. R. A. GRISWOLD and FRANKLIN JELSMA, Arch. Surg. **15**:45 (July) 1927.

Griswold and Jelsma outline the autopsy results in eight cases of chronic subdural hematoma seen in the Louisville City Hospital. The source of the original hemorrhage in the cases was not clear. They presume that following cranial trauma, often slight, possibly with some predisposing vascular lesion, bleeding occurred from a small vessel of the dura or from one of the veins entering the sinuses. This might be a single large hemorrhage, repeated small hemorrhages, or slow constant oozing. Reaction to the hemorrhage follows approximately the same course as in extravasation of blood elsewhere; namely, reaction of leukocytes and fibroblasts with consequent organization. The inner membrane is formed by growth of fibroblasts and endothelium from the dura at the edges over the bridge formed by the clot. The exception in these cases is the formation of spaces lined with endothelium in the organizing tissue just beneath the dura. It is probable that these spaces forming cystlike structures are formed by the proliferation of detached bits of dural endothelium in the clot, as may occur on other serous or epithelial surfaces. Many of these spaces contain blood, and in some sections they may be seen to connect with capillaries. This connection may occur by fusing, during the simultaneous formation of these spaces and the capillaries growing into the clot, when cellular proliferation is active. The occurrence of repeated hemorrhages with recurrence of symptoms may be explained by rupture of these blood-filled spaces during sudden changes of pressure, as in coughing or straining. In their cases, definite histologic evidence of repeated hemorrhage was not evident, though in some portions of the old clots the blood cells were remarkably well preserved, and in one case there was recurrence of symptoms.

Histologic differences were not apparent between the cases with history of trauma, and those in which such history was not elicited. In the recent, actively organizing clots the endothelial cells lining the cystic spaces were more scattered and irregular, capillaries were more numerous, and fibrous tissue was looser than in the older and more fully organized clots. In general, the clots in cases without a history of trauma appeared older and more nearly healed. The cases with definite relationship to trauma, however, had older and better organized fibrous tissue and endothelium than those in which there was not a history of trauma. The authors believe that features, such as development of endothelium, which are usually considered as differentiating chronic subdural hematoma and chronic pachymeningitis hemorrhagica interna, are rather differences in degree of organization than differences in type. The high concentration of bilirubin in two of these clots (thirty and twenty times that in the blood from the heart) and crystals of hematoidin in others indicate that bile pigment is formed during their absorption and organization.

The factors of alcoholism and insanity which accompany so many of the cases of pachymeningitis hemorrhagica reported must be taken into account in evaluating the apparent absence of injury. Alcoholism was prominent in

five cases in this series, and contributed to the trauma in two. The drunkard with contusion of the scalp who does not remember receiving an injury is not uncommon. A psychosis appearing in so many of the known traumatic cases explains the frequent occurrence of pachymeningitis hemorrhagica at necropsy in asylums, since the mental derangement is a result rather than a cause of chronic subdural hematoma. The degree of trauma necessary to produce this lesion, but not sufficient to cause fracture in any case in this series, may be so slight that it requires special effort on the part of the examiner and the patient to obtain a history of injury. In the old case in the alcoholic patient and in the insane person, it is especially difficult to get such information. It is probable that most, if not all, cases of so-called spontaneous pachymeningitis hemorrhagica have a beginning in a forgotten injury.

Symptoms of chronic subdural hematoma fall into two classes: those due to general increase in intracranial pressure, as headache, vertigo, vomiting, slow pulse and choked disk; and those due to local disturbance, as paralysis, sensory disturbances (rare), convulsions and aphasia. In addition, there may be those of meningeal irritation, such as stiff neck. These signs may occur in almost any combination, and, besides being variable and fleeting, are likely to be atypical and incomplete. This series is characterized by a latent period of varying length as a rule. Headache followed by vertigo, vomiting, psychosis and coma is the common course. Choked disk was not found in the four cases observed recently, and was indefinite in one case. It is often surprising that there are so few physical observations. Terminal lobular pneumonia is common. Increased reflexes, spasticity of various groups of muscles and disturbances of the third and fourth cranial nerves are the chief neurologic observations. The spinal fluid is usually normal in all respects, though it may be xanthochromic, or it may contain blood in those cases in which the arachnoid was injured. The temperature varies little from normal, though it is usually slightly subnormal toward the end. The pulse is often a pressure pulse.

Diagnosis depends on a history of cranial trauma, often slight, followed by a variable latent period. It may be impossible to elicit a history of injury. Following this is a period of headaches, continuous or intermittent, increasing in severity, then psychosis, coma and death. If the diagnosis is made early and surgical treatment instituted, the prognosis is fairly good.

GRANT, Philadelphia.

AMAUROTIC IDIOCY AND LIPOID CELL SPLENOHEPATOMEGALY. MAX BIELSCHOWSKY, J. f. Psychol. u. Neurol. **36**:103, 1928.

Recent clinical and anatomic observations would seem to show that in amaurotic idiocy the involvement of the nervous system is occasionally only a component of a general disease of the organism, in which a disturbance of the lipoid metabolism is of the greatest pathogenic significance. Gaucher's disease and Niemann-Pick's lipoid cell splenohepatomegaly are also two clinical entities in which disturbances in lipoid metabolism are important features. Investigations during the last two decades have shown that in Gaucher's disease metabolic disturbances are not limited to the spleen, but also involve the entire lymphatic and hemopoietic apparatus of the organism. The characteristic feature in the microscopic changes of the disease is the formation of peculiar cells, the so-called Gaucher cells in the parenchyma of the spleen, liver, lymph nodes and bone marrow, as well as the grotesque enlargement of the spleen and liver. The disease may affect persons at any age, and although racial predisposition does not exist, familial occurrence of the condition has been repeatedly observed. The Gaucher cells frequently are found in the form of large nests; they are derived from the reticulo-endothelial apparatus, and their peculiar appearance is due to the deposition of a substance which is chemically a kerasin belonging to the group of sphingogalactosides. Pick also emphasized that the organs in which the Gaucher cells are deposited are pigmented by hemosiderin and that in some cases a general hemochromatosis may be found

throughout the lymphohemopoietic system. This observation, however, is only of secondary importance.

Little attention had been given to the nervous symptoms occurring in Gaucher's disease until Oberling and Woringer pointed out that when the disease affects nursing infants, regularly, recurring cerebral symptoms are a striking clinical feature; these have never been observed in adults affected by the disease. The nervous symptoms develop rapidly and at the same time that the spleen begins to enlarge. In one of the patients, the parents noted that at the age of 5 months the child became listless, and the development of all its static functions became arrested. In other words, the nervous symptoms could be divided into two groups: psychic and motor. The neurologic component of the syndrome in these infants gives one the impression of decerebrate rigidity with preservation of only the vegetative functions. Postmortem examination of the brain showed extensive cortical changes in both cerebral hemispheres, with unusually severe involvement of the parietal and occipital lobes. The sections were re-examined by Bielschowsky who confirmed Oberling and Woringer's observations. The medium-sized and large pyramidal cells in the third layer and in the sixth layer in the occipital cortex showed the greatest involvement. Every microscopic field was full of shrunken cells, and many of these also showed vacuolization. As far as one could tell from the microscopic examination, the content of these cells did not consist of phosphatids as is the case with the diseased ganglion cells in amaurotic idiocy. Bielschowsky bases his conclusion on the fact that these cells did not stain well with iron hematoxylin or with Weigert's hematoxylin. He believes, however, that in spite of this it is not at all impossible that there may be a deposit of a peculiar kind of lipoid resembling kerasin within the parts of the cells that are full of vacuoles.

These observations, according to the author, are significant because they seem to show that in a disease of the lipoid metabolism well recognized clinically, anatomically and chemically, the nervous system is also involved and that the substratum of the nerve involvement is a change of certain cell types in the cerebral cortex, consisting of swelling and vacuolization. The fact that similar nervous manifestations appear so early in the clinical course of Niemann-Pick's splenohepatomomegaly would also seem to be in favor of the idea that the changes in the ganglion cell in Gaucher's disease are not a secondary phenomenon, but are of the same pathologic significance as the changes in the cell in the spleen, liver, lymph glands and bone marrow. As a matter of fact, one of Pick's cases of splenohepatomegaly, proved anatomically, showed nerve symptoms clinically which were practically identical with those noted in the Tay-Sachs form of amaurotic idiocy. The microscopic changes of the brain and cord in this case were also the same as in amaurotic idiocy, except that the vascular tissue apparatus in the brain was also involved—an observation usually not encountered in Tay-Sachs' disease.

A careful study of the problem does not leave any doubt that in Gaucher's disease and in the Niemann-Pick type of splenohepatomegaly, as well as in amaurotic idiocy, there is a close relationship between the lipoid metabolism and the pathologic changes in the nervous system and in the other organs. If future studies confirm this view, the hyaloplasm theory of Schaffer will have to be disregarded and the conception that amaurotic idiocy is a heredodegenerative disease, rejected. In any event, this aspect of the problem seems to open up a new field for research. Bielschowsky, therefore, urges that in all forms of amaurotic idiocy careful postmortem anatomic as well as chemical examinations be made of the internal organs, and that in splenohepatomegaly the nervous system be subjected to similar investigation. Such studies may, in the future, yield valuable information as to fundamental metabolic changes and their possible causal relationship to the diseases in question.

KESCHNER, New York.

CONCEPTION OF DISSOCIATION. BERNARD HART, Brit. J. M. Psychol. **6**:241, 1926.

Psychology has long been concerned with the general concept of the division of the mind. In fact, a great deal of psychologic thinking has been devoted to

splitting the mind up into compartments with more or less remote connections and studying the separate phenomena. Janet was responsible for the development of the present psychologic concept of dissociation to explain the phenomena found in hysteria and hypnosis. He observed certain mental facts leading an existence apparently independent from the stream of conscious activity. The connection between these apparently split-off activities and consciousness was demonstrated by automatic writing and hypnosis. Dissociation formed the essential factor of hysteria and hypnosis, the latter being regarded as an artificially produced form of hysteria. For Janet, dissociation is a splitting of mind elements into different masses which normally adhere and form a coherent whole. It is a spatial conception which distorts the facts. For example, it is frequently observed that the person in hypnosis has a great many of the same memories observed in the conscious stream. There are common elements in the two states and not a clean schism. An experience may pass out of consciousness and be revived in a hypnotic state and be a part of a fugue or some hysterical phenomenon. The apparent dissociated status of this memory refers only to the deprivation of associative variations with the level of awareness. Fundamentally, it still forms an integral part of the mind. An example is cited to show how the activity of an apparently dissociation stream is influenced by suggestion introduced in another state apparently quite isolated. Something more than the spatial conception is necessary to understand the factors which influence both states and yet apparently belong to neither.

Abandoning the spatial terminology of Janet helps to clear up the problem. Dissociation in reality does not create spatial divisions of mind; it does not separate it into pieces but produces certain patterns each one of which may have certain definite characteristics, but which may form a part of any number of units. "Instead of regarding dissociation as a splitting of conscious material into separate masses, it must be regarded as an affair of gearing, the various elements of mental machinery being organized into different functional systems by throwing in the appropriate gear."

The functional concept and the spatial concept differ radically. The spatial concept regards dissociated consciousness as an accretion of elements, simple in hysterical anesthesia and involving only a few, and complex in multiple personality when a sufficient number of elements have accrued to make a new personality. The functional concept, on the other hand, stresses the synchronizing integrating activity which enables these elements to cohere.

The attempts to establish lines of division in the continuity of the mind have been really divisions of consciousness. Janet's subconsciousness is a division on the phenomenal plane and is purely descriptive of the observed facts, whereas the unconsciousness of Freud is a conceptual construction and is created to explain phenomenal facts which Janet only describes. There is a fundamental difference in the methods of these two schools of thought. Janet classifies and describes phenomenal facts, whereas Freud attempts to formulate laws that will explain the same facts. He goes one step further than Janet in the three processes of science described by Pierson, namely, (1) observation and recording of phenomena; (2) classification of the same, and (3) the construction of laws to explain the phenomena. Freud goes further in his conceptual point of view and divides the mind into the ego and the id, with the ego forming the coordinating factor of the mind and the id, the unconscious motivator of the phenomena observed on the ego level. These conceptual formulations of Freud lie on an entirely different methodologic plane from the phenomenal conception of Janet, and the distinction of plane must be rigidly enforced if confusion of thinking is to be avoided.

The followers of the Janet school have manifested more interest in the problem of multiple personality than have the followers of the freudian school. The psychoanalytic literature on the subject is meager. The contention is that the multiple personality is an artefact which grows extensively under the hypnotic method of investigation. The emphasis is on the examination of the symptomatic behavior. The freudian becomes interested less and less in the symptom — the actual phenomena of dissociation — and more interested in the antecedents and

determinants, and the term dissociation has little place in this dynamic concept. Repression is an active purposeful process having varying degrees of success. When it fails, the repressed material comes back in the form of symptoms which can be described as dissociated but which still form a living part of the individual. This marked difference between descriptive psychiatry and dynamic psychiatry—the one describing, the other explaining—is a fundamental one. Emphasis on the dynamic aspect has relegated the symptom to a position of secondary importance.

ALLEN, Philadelphia.

THE AETIOLOGY AND TREATMENT OF ACUTE POLIOMYELITIS. S. A. K. WILSON, Lancet **1**:11 (Jan. 7) 1928.

A definite relationship has not yet been established between the mildness or the severity of the initial syndrome of acute poliomyelitis and of the paralytic consequences. This disease presents all the characters of a specific infection and seems to be independent of any other. Poliomyelitic symptoms supervening in the course of another febrile disease are to be regarded as coincidental or as exceptional localization and action of the febrile virus. Seventy-five per cent of all cases develop in children who have not passed the age of 9 years. In outbreaks of epidemics the incidence in youths and adults tends to increase in comparison with that of sporadic outbreaks. The possibility of intra-uterine infection has been discussed by Batten and others, and a case is known in an infant of 12 days. The disease has appeared at intervals all over the world; it has not spared the colored races. Hereditary and familial "taints" may be disregarded as predisposing factors. Familial involvement varies considerably in different epidemics. The disease occurs mostly in the summer and autumn months.

The fact that in an epidemic at Cortland, N. Y., all eight persons who were affected drank milk from a farm on which a case of poliomyelitis had occurred, shows that case to case infection is not the sole means of dissemination. Notwithstanding this, direct contagion from one human being to another is accepted as the chief mode of spreading the disease. Evidence points to the conclusion that the virus is carried in the nasal, buccal and faucial mucous membrane of persons who have had the disease or who may simply be carriers. Taking all this into consideration, the fact still remains that the condition never runs riot in schools, and bed to bed contagion in hospitals is negligible. Direct infectivity in the experience of the author is greatest during the incubating and preparalytic stages. When the virus reaches the nervous system it becomes "tucked away" and is less communicable.

The following practical considerations may be deduced from the foregoing. A patient in whom the disease is developing is infective and should be isolated. A patient who has run the risk of infection, and whose case may be purely abortive, is equally infective. A patient in whom paralytic phenomena have appeared is possibly, or even probably, past the stage of infectivity by direct contact. Those who come in contact with infective cases may become carriers and yet may not show any sign of the disease. Such persons may regard themselves as having passed out of danger of disease after three weeks, but how long they may remain a danger to others is more difficult to estimate.

In treatment of persons who come in contact with patients, efforts must be made to destroy the organisms in the upper respiratory passages. Potassium permanganate (1:5000), peroxide of hydrogen (1 per cent), solution of chlorinated soda (0.5 per cent) or some other chlorine-containing preparation is advisable as a douche or gargle. When paralytic symptoms appear, these are valueless. The sole specific treatment consists of intraspinous injections of immune serum. Immunity following an attack remains for an indefinite time. From 30 cc. of immune blood the serum is separated, warmed and injected by the lumbar route in amount corresponding to the quantity of fluid withdrawn, from 4 to 12 cc. The treatment may be adopted daily for some days and should be begun as soon as possible. The preparation of animal serums is at present

difficult. Streptococcic poliomyelitis serum obtained from immunized horses may be of value, used intramuscularly or intravenously, though the author has had no personal experience with it. Other methods of therapy used are methenamine and a combination of spinal radiotherapy and diathermy. Absolute rest in bed for at least three weeks and complete relaxation of the involved muscles, if necessary by splints and plasters, are of importance. The nutrition of the muscle groups should be maintained by physical means, first by warm baths and friction, later by light massage and movements. Electrical stimulation is less advantageous and is not called for at an early stage. Physiotherapy should be persisted in to obviate contractures, and orthopedic measures may be called for after a year.

PETERSEN, Montreal.

PROGRESSION AND REGRESSION IN TWO HOMOSEXUALS. T. A. ROSS and R. D. GILLESPIE, J. Neurol. & Psychopath. **7**:313 (April) 1927.

The authors stress the need for more case material if psychopathology is to stand. They do not make any claims to be orthodox freudians but agree that many of the features of the two cases studied are difficult to explain except on a freudian theory. They believe that certain fundamentals of Freud's views are true, but that on these he has raised a superstructure which is of less sound material.

In one of the patients, homosexuality was merely a symptom and had a time of beginning, a period of growth and a time when it faded and disappeared. This patient, a man, aged 47, was thoroughly masculine in appearance and rather careless in dress. He was a highly cultured and a successful business man and had heard much of psychoanalytic doctrine. So far as he could remember when first examined, he had never taken any interest in women. Philanthropic work had led him to become interested in boys' clubs, but not until a few years before being studied did he have any conscious homosexual desires. From the time he was about 45 he had increasing realization of abnormal impulses. He became depressed and finally made an abortive attempt at suicide. He regarded himself as of purely feminine type, but there was evidence of an active homosexual trend. After a month of treatment, which included attempts to combat self-loathing and depression, he remembered an event when he was 15 years of age in which he made a heterosexual approach and was interrupted with circumstances causing great embarrassment. The whole affair had rapidly been repressed and a delayed sex-consciousness was further delayed. Not long after this memory was recalled, normal heterosexuality unfolded itself with inconvenient rapidity. As there is considerable pessimism regarding homosexuality the occurrence of such a change is worth recording. It is not wise to say that nothing can be done or to make promises that one can transform a sufferer from this anomaly into a normal heterosexual person.

In the second case, homosexuality did not emerge into consciousness till the patient was in his prime. It persisted in consciousness for a time and then was projected. The report shows in detail the psychopathologic development of a paranoid psychosis. There was unusual opportunity for observing the growth of mental abnormality from an early stage. The patient had been a delicate, "high-strung" child. He began work at 19, became a successful manager of a business and later married. He was always "fussy" and overscrupulous in everything. He worried about every possible calamity. At 52 years of age, he became "slack" in his work; later he had an attack of influenza. Following this illness he ceased marital relations. For about a year, he developed depressive and paranoid ideas. After coming under treatment at the age of 55, his preoccupations became entirely homosexual. Many delusions developed and at last accounts he was becoming worse. He fulfilled well some of the conditions of Freud's analerotic character, although he was not parsimonious. He had not read anything about psychoanalysis. The

details of this case also furnish data for psychopathologic theory and are thoroughly discussed. It is suggested that so-called "unconscious" wishes or ideas are originally conscious but may be treated in various ways by the person who entertains them. The normal person either treats them with repugnance and can thrust them from him because his other wishes and interests are stronger or he acknowledges them frankly as part of himself. The psychotic person cannot do either. He has to abhor what at the same time he ardently desires, and projection occurs as a compromise between the desire and the fear.

FAVILL, Chicago.

THE MYELOARCHITECTONIC STRUCTURE OF THE HUMAN TEMPORAL LOBE WITHIN THE SYLVIAN FISSURE. EDUARD BECK, J. f. Psychol. u. Neurol. **36**:1, 1928.

The isocortical portion of the temporal lobe region is divided by the author as follows: 1. Subregio temporopolaris, (*a*) pars medialis; (*b*) pars lateralis. 2. Subregio temporalis superior, (*a*) pars medialis; (*b*) pars lateralis. 3. Subregio parainsularis. 4. Subregio temporalis transversa prima, (*a*) pars temporalis transversa prima intima; (*b*) pars temporalis transversa prima interna; (*c*) pars temporalis transversa prima externa; (*d*) pars temporalis transversa prima extrema; (*e*) pars temporalis transversa prima lateralis. 5. Subregio temporalis transversa secunda, (*a*) pars medialis; (*b*) pars lateralis. 6. Subregio temporalis transversa tertia, (*a*) pars medialis; (*b*) pars lateralis. 7. Subregio temporoparietalis.

Examination of these subregions orocaudally shows a continuous increase in the content of myelin fibers. This increase is never sudden; it consists of a gradual change in the cortex. The gradation is not only from less marked to more marked, but also from more marked to less marked. All border lines are sharply delineated, and the changes are noted in all layers. The author points out further that the right hemisphere contains precisely all fields that the left hemisphere does. Certain differences in the size of the various areas as well as certain displacements in position are noted, but these are probably due to poor technic in preparing the sections; in a great many instances, however, these variations, especially in the right hemisphere, were noted even when the sections were prepared with great care. Whatever differences exist are only quantitative in nature.

The region described is generally assumed to be part of the center for the reception of speech. This presupposes a predominance of the left temporal lobe in right-handed persons. While this cannot be denied on clinical grounds, nevertheless, there is not any anatomic evidence to confirm it. The following conclusions may therefore be drawn: (1) this region has nothing to do with sensory speech, the basis for which must be sought in different parts of the temporal lobe; (2) as the right hemisphere is structurally identical with the left, the functions of the former must be similar to those of the latter. The function which corresponds to this hypothesis is undoubtedly that of central hearing which must *a priori*, presuppose a similar structure of the left and right hearing centers. The hearing center, however, is not within the entire region described in this communication but is primarily to be found only in the transverse areas. This theory is substantiated by the following facts: 1. The transverse areas not only are the richest in myelin of all the areas in the region of the temporal lobe but also are the most differentiated. They also lie nearest to the acoustic radiation. In this region also are included parts of the second transverse convolution, especially in the caudal portions. 2. The transverse areas can also be found in chimpanzees, in *Cercopithecus* and even in the dog. The chimpanzee, especially, has an anterior transverse convolution which shows quite a complex structure. In the dog, the subdivision into subareas is naturally much more primitive than it is in *Cercopithecus*. 3. Even though the temporal pole in the chimpanzee is poor in myelin, it is differentiated from the temporal pole in man by the fact that in the former it is internodensior, whereas in the latter it is exquisitely externodensior, and practically singulostrial.

KESCHNER, New York.

ANGINA PECTORIS: TREATMENT WITH PARAVERTEBRAL ALCOHOL INJECTIONS. JAMES C. WHITE and PAUL D. WHITE, J. A. M. A. **90**:1099 (April 7) 1928.

Up to 1927, at the Massachusetts General Hospital, cervical sympathectomy as a last therapeutic resort for obstinate angina pectoris had left much to be desired. Having read the recent report of Mandl and Swetlow, the authors performed paravertebral alcohol block on the upper five left dorsal nerves in five patients, and observed them for from four to thirteen months after injection.

The most important cardiac afferent fibers run by way of the upper, middle and lower cardiac nerves to the cervical sympathetic trunk, and many fibers come also into the stellate ganglion and even further down into the dorsal sympathetic chain. On the other hand, the rami communicantes of the upper dorsal nerves are the chief communications between the cervicodorsal sympathetic chain and the cord. These rami are the ones which it is attempted to block by paravertebral injection, the technic of which, as described by the authors, follows:

A 10 cc. glass syringe and a set of thin, sharp needles from 8 to 10 cm. in length are the only equipment needed. A rubber depth marker for each needle is used. The patient lies on his right side, as he does when lumbar puncture is performed, and the back of the thorax and shoulders is thoroughly cleansed with alcohol and iodine. The spinous processes of the upper five dorsal vertebrae are marked with acriflavin. A second series of marks is made 4 cm. to the left of each of the previous marks. A solution of 1 per cent procaine is injected intradermally at each of the latter points. Then the needle is inserted perpendicularly to the back plane until the underlying rib is felt (for from 3 to 5 cm.). The tip of the needle is slipped by the lower edge of the rib and then rotated to point caudally and medially 45 degrees. It is then advanced exactly 2 cm. All five needles are thus inserted and aspirated (to be sure there is no blood nor spinal fluid in them), and then 5 cc. of a solution of 1 per cent procaine is injected through each.

Within ten minutes of this injection there should be anesthesia from the midline in the back to the sternum, and from the fifth intercostal space up to where the descending branches of the cervical plexus overlap the three upper ribs. If the first and second nerves have been properly blocked there should be good anesthesia of the axilla extending a few centimeters down the arm along with the Horner syndrome. As soon as anesthesia is complete, 5 cc. of 85 per cent alcohol is injected into each needle; then the needle is withdrawn.

The authors report five cases rather briefly. When the nerves began to function again the patients were always hyperesthetic and experienced considerable discomfort for from two to six weeks following the injection. The Horner syndrome may last for months. The length of time that pain will be relieved is still unknown (the first patient is doing well after thirteen months).

The expectation of life is in no way affected by the relief of pain. There is no reason for not performing a second injection. Injection on the left side has no effect on cardiac pain referred to the right side.

Two patients were completely relieved of left-sided attacks but had mild attacks on the side into which injection had not been made. Two others had severe attacks which were converted into mild and less frequent attacks. The fifth patient was relieved only for a few days. There were no harmful complications, but all the patients complained of hyperesthesia of the injected nerves lasting for from two to four weeks.

CHAMBERS, Syracuse, N. Y.

FURTHER EXPERIMENTS ON ALTERATION OF THE DIRECTION OF GROWTH IN AMPHIBIAN SPINAL NERVES. S. R. DETWILER, J. Exper. Zool. **51**:1 (May 5) 1928.

When the right anterior limb rudiment of *Amblystoma* embryos is excised, and an optic vesicle with the adjacent nasal placode is grafted three or four segments caudal to the normal limb site, spinal nerves from higher levels grow caudally toward the graft. The fifth spinal nerve extends caudally a considerable distance to the region of the differentiating olfactory organ and in one case it actually

penetrated the nasal sac. The sixth spinal nerve also grows toward the olfactory organ, or toward the more caudally lying grafted eye. The seventh nerve is usually attracted toward the grafted eye. In several cases in which a limb regenerated in the orthotopic position, the fifth nerve bifurcated—one branch going cephalad to the regenerant and the other caudad to the region of the olfactory organ.

When the anterior limb is excised and a tail bud is grafted four segments caudal to the normal limb site, spinal nerves from slightly higher levels than that occupied by the graft show some caudal growth in several cases. In no cases, however, is there any connection of the host nerves with the musculature developing within the graft. Such grafted tails develop an isolated piece of spinal cord with ganglia and peripheral nerves. These nerves supply the tail musculature. Even when a tail bud is substituted for the limb rudiment, there is no growth of the brachial nerves into the grafted tails. The caudal growth of spinal nerves toward an implanted nasal placode or eye is much the same in character as when the anterior limb rudiment is shifted to the same position. This indicates that the differentiating graft in both types of experiment exerts a similar attraction on the nerves. The results strengthen the view that when brachial nerves grow caudally considerable distances to a grafted limb, they are attracted by forces which are nonspecific for limb nerves, and it may be that any system which is undergoing high physiologic activity may attract nerves which are growing in the general vicinity of such a system. The failure of the differentiating grafted tails to attract spinal nerves is viewed as resulting from the fact that the developing tail musculature becomes sterilized by nerves growing to it from the isolated spinal cord which develops within the graft.

Tail buds grafted to the side of the body grow out at various directions, depending on the orientation of the graft, although the early growth seems to be somewhat affected by the surrounding tissue. A complete neuromuscular mechanism develops in the tails and is functionally isolated from that of the host. Tactile stimulation applied to the graft results in reflex responses which are carried out independent of host movements. Several instances of "spontaneous" movements in grafted tails have been noted. The attraction of ventral spinal nerves by strange tissues (eye and nasal placode grafts) without actual union of the nerves strengthens the view that in the general growth and in the peripheral connections of nerves during normal development, different forces are acting. Those concerned with the general direction of growth appear to be of a very general, nonspecific character, whereas those concerned with actual connections of the nerves with their end-organs appear to be much more specific in nature.

WYMAN, Boston.

THE NUCLEUS AMYGDALAE IN MAN. PAUL HILPERT, J. f. Psychol. u. Neurol. **36**:44, 1928.

A study of the cyto-architectonic and fiber connection of brains of fully developed human beings, as well as those of fetuses in various stages of development showed the following: The nucleus amygdalae (archistriatum) in man is a highly developed ganglion consisting of six different cell areas (nuclei) situated at the oral end of the inferior horn in the region of the hippocampal gyrus. The gyrus semilunaris, the semiparietine cortex of which is regarded as the cortical portion of the nucleus amygdalae, shows four areas—the areae periamygdalares *pa* 1 to 4—whereas the areas *Pam* 1β and 1γ (Rose) belong to the early maturing cortical areas of the hippocampus; these are probably derived from the matrix of the olfactory cavities. The ventral nucleus of the nucleus amygdalae is surrounded, anteriorly and laterally, and traversed by the corticopetal optic tract, the old fasciculus longus inferior. At all points, the nucleus amygdalae can be clearly separated from the substantia innominata which surrounds it laterally. The lateral border of the regio peri-amygdalaris is made up of the area praepyriformis and the area diagonalis; caudally this region abuts against the formatio ammonis of the uncus and mesially against the area semi-annularis.

The following centripetally leading fiber formations of the nucleus amygdalae were established: (1) fasciculus thalamo-amygdalaris, the old fascia thalamicus inferior; (2) fibers from the lateral olfactory root; (3) fibers from the deep fiber layers of the ventricular wall, which probably originate from the corticofugal optic tract; (4) fibers from the oral portion of the cingulum; (5) early maturing fibers from the taenia semicircularis, which join the nucleus amygdalae to the substantia perforata anterior.

The following centrifugal connections were made out: (1) fasciculus amygdalo-ammonalis, the most important and most extensive centrifugal fiber connection; (2) fiber tracts which pass through the substantia innominata and join Türck's bundle (they probably go together to the pons and are in some relationship to the cerebellum); (3) late maturing coarse fibrous portions of the taenia semicircularis, which represent perhaps the strongest association tracts of the nucleus amygdalaris.

The following commissural fibers were established: (1) direct fibers to the anterior commissure; (2) indirect fibers to the same commissure by way of the taenia semicircularis; (3) fibers possibly going between the nucleus amygdalae and the tapetum—the corpus callosum.

As far as one can draw conclusions from these anatomic facts and from some few clinical observations that have been made, it would seem that the nucleus amygdalae is a regulating center for the undoubted motor function of the cornu ammonis. This relationship is analogous to that of the function of the thalamus to the striatum and pallidum. The cornu ammonis, which is predominately in relation with tonic centers, might possibly be the starting point for so-called principal or common movements, especially for automatic defensive movements. If this is true, one could also readily perceive its relationship to the epileptic convulsion.

KESCHNER, New York.

THE TREATMENT OF THE SEQUELS OF HEAD INJURY. W. RUSSELL BRAIN and HUGH CAIRNS, Lancet **1**:668 (March 31) 1928.

Many cases of persistent cerebral contusion can be prevented if the injury is adequately treated in the acute stage. Treatment in late cases is based on the same principles. Rest in bed is essential. Sometimes headache may be prevented if the patient sleeps sitting up with his head and shoulders resting on pillows. Analgesic drugs may be used. Hypertonic solutions are of great value and the preferable route is the intravenous, by which injections can be given at intervals of four or five days if necessary. If these measures fail, subtemporal decompression may be resorted to, on the right side if there are no localizing signs, on the side involved if there are localizing signs, and in conjunction with an osteoplastic flap if one wishes to examine the site of the contusion. Recently, introduction of air into the subarachnoid space in the lumbar region has been employed in this condition.

One understands traumatic neurasthenia as a state of anxiety neurosis which occurs in the absence of, or outlasts recovery from, an organic lesion produced by an accident. In its later stages, especially when complicated by litigation, it is temporarily incurable. It is preventable and, when it first develops, amenable to treatment. Care must be taken to avoid suggesting incapacity to the patient, and positive suggestions of a speedy recovery must be made. His symptoms should be explained to the patient, and his weakness or giddiness explained as a natural result of confinement to bed. Physical exercise should be begun at the earliest possible moment. An attempt should be made to obtain the sympathetic cooperation of the employer or foreman, who can do much to remove the fear of a breakdown following resumption of work. A "light job" to start with may be of great value. The problem is complicated by the fact that persistent cerebral contusion is an organic lesion, usually without abnormal physical signs, that may cause symptoms of anxiety neurosis and be mistakenly diagnosed as neurasthenia.

About 5 per cent of patients with injuries of the head develop epileptiform convulsions. It is suggested that these are not the result solely of the injury, but

are probably the outcome of a predisposition to epilepsy precipitated by the trauma. The treatment should be medical and the same as that used in idiopathic diseases. If after a few months there is no response to treatment, operation may be considered. Exploration should be made at the site of the focal lesion. In some cases benefit has followed excision of, or injection of alcohol into, a localized area of the cortex, but too much must not be expected of these measures. Subdural hematoma may not give rise to symptoms for weeks or months after the original injury. It may be mistaken for tumor, and its signs are those of slowly increasing intracranial pressure, with slight and variable focal signs. The clot should be removed by operation and the other side of the brain explored, as this condition is frequently bilateral.

PETERSEN, Montreal.

CONCERNING THE ELECTRICAL EXCITABILITY OF THE FETAL MUSCULATURE. M. MINKOWSKI, Schweiz. Arch. f. Neurol. u. Psychiat. **22**:64, 1928.

The writer investigated the electrical excitability of the muscles of twenty fetuses, ranging in length from 3.5 to 35 cm., i. e., from the ages of 2 to 7 months. The specimens were examined promptly after delivery and kept at body temperature, since chilling in itself may change the reactions both quantitatively and qualitatively. Minkowski found that the fetal musculature responds to stimulation by both the galvanic and the faradic currents after the third month. The response to the faradic current is always tetanic and resembles that noted in the adult. The response to the galvanic stimulus, however, varies. There may be a lightning-like response, a somewhat prolonged response, without tetany, and, as is usually the case, a tetanic reaction which persists during the entire time the galvanic current is applied. The muscle may be excited on stimulation of the nerve trunk with the galvanic current relatively early in life, i. e., from the fourth month of fetal life. This is interesting, as the nerves are at this time still without a myelin sheath. The slow response to galvanic stimulation resembles the response seen in a muscle which has been subjected to asphyxia, cooling or injury to its motor nerve.

The facts that a myotetanic reaction to galvanic stimulation occurs in many fetal muscles, that this reaction occurs in muscles which are less excitable, and that it appears toward the end of the period of observation, suggest that in fetal muscle there is a more primitive and resistant form of direct aneural irritability. Von Frey found a cathodal closing tetanus almost regularly in frogs which had been kept at a temperature below 10 C. for a time. The contraction of smooth muscle to the electric current is also slow. The fetal tetanic reaction bears certain resemblances to the myotonic reaction of Thompson's disease. The continued contraction for the duration of the galvanic current, as well as the faradic current, is observed in fetal muscle, but the persistence of the contraction after interruption of the current is not seen here as it is in Thompson's disease.

The question whether this response bears any relationship to the anatomic structure of the muscle naturally presents itself. Weiss found a relationship between the histologic development and the functional character of fetal muscle in the frog and axolotle. He arrived at the conclusion that embryonic muscle, because it has either no or very little differentiated myofibrillary substance and a predominance of sarcoplasm, has a contraction which is tonic in nature. It is only with the development of myofibrils that short twitches become possible, and that the amplitude of the twitch rises with the intensity of the stimulus.

WOLTMAN, Rochester, Minn.

ANNUAL REPORT OF THE NEUROPSYCHIATRIC CLINIC OF MUNICH. Arch. f. Psychiat. **80**:1 (March) 1927.

This article is a report, under the heads of the different departments, of the activities in the Munich clinic during 1925. The data are necessarily condensed and do not lend themselves to a comprehensive abstract. Professor Bumke discusses briefly the general situation and changes in the clinic, stress-

ing especially the point that a neurologic department was added to the previously more or less purely psychiatric clinic. Kahn reports experiences with psychopatnies and psychogenic reactions as well as with manic-depressive psychoses; this report is predominantly statistical but there are short presentations of cases. There is a tendency to emphasize the purely clinical point of view, and a leaning toward the Kretschmer physique-character type of studies. Jahrreiss discusses the paranoic and paraphrenic conditions and epileptic reactions and diseases; psychopathologic and hereditary studies were undertaken and brief abstracts are given of cases presenting positive data. Jaspersen presents a study of suicidal attempts from a diagnostic and characterologic point of view. Kant reports on inebriates, intoxications and symptomatic psychoses; special studies were undertaken to determine how much of the mental reaction was caused by the organic factor and how much was dependent on a previously morbid personality. The schizophrenic cases reported by Braun, were studied mostly from a clinical and hereditary point of view. A brief discussion of the therapy is given, with a rather pessimistic attitude. Bostroem reports experiences with general paralysis and cerebral syphilis and in the neurologic division. The discussion of the differential diagnostic and clinical features in these organic conditions in a large psychiatric clinic is of especial importance. Wilhelmi discusses the climacteric and arteriosclerotic-senile psychoses; Zech, feebleminded persons and cretins, and Johannes the outpatient department of the neurologic clinic. All are more or less statistical reports with some presentation of clinical data. The report concludes with a review of the work in the laboratories by Spatz (neuropathologic) and Wuth (chemical).

MALAMUD, Foxborough, Mass.

THE ANATOMY AND PHYSIOLOGY OF THE LABYRINTH OF THE EAR AND OF THE EIGHTH NERVE. PART 2. R. LORENTE DE NO, Trav. du lab. de rech. biol. de l'université, Madrid, July, 1926.

In a former publication (abstr., ARCH. NEUROL. & PSYCHIAT. **18**:281 [Aug.] 1927) of which the present contribution is the continuation, the author made a special study of the tonic labyrinthine reflexes. This second part of the work is particularly devoted to the anatomic and embryologic problems involved in the subject.

A series of rats were used for the investigation. It was found that the vestibular organs of mammals were built on the same plan as those of birds. This confirms Cajal's views which had been questioned by Kolmer. The peripheral distribution of the acustic nerve was also studied, and various labyrinthine organs were found represented in Scarpa's ganglion. Five separate histologic structures were identified in the ganglion, differing mainly in the respective size of the constituting cells. A definite correlation exists between these five cell groups, on the one hand, and the different organs of the labyrinth, on the other. Thus, the cells of the pars magnocellularis anterior correspond to the anterior and external ampullae and to a definite region in the utricle. The pars magnocellularis posterior contains the cells for the posterior ampulla, and the pars parvicellularis anterior, those for the macula of the utricle.

In the trunk of the cochlear nerve the author found cell clusters in the vicinity of the porus acusticus internus which, he thinks, are in close functional association with the ventral intramedullary nucleus of this nerve.

In studying the process of myelinization, it was found that the vestibular nerve is first to develop a myelin sheath. Then follows the cochlear nerve. But in the subsequent stages of development, the myelinization of the cochlear pursues a much quicker course than that of the vestibular. In this manner, the process commences earlier in the vestibular but terminates earlier in the cochlear nerve.

There follows a discussion of the question whether, on embryologic grounds, the nervous elements can be said to initiate the development of the epithelial

parts or vice versa. In this connection, Cajal's theory of a selective neurotropism is touched on but rejected. The author's conclusions are that both nerve fibers and cellular structures develop independently of each other.

Low, Chicago.

THE ARCHITECTONIC STRUCTURE OF THE CEREBRAL CORTEX (ISOCORTEX) IN THE DOG. M. GUREWITSCH and G. BYCHOWSKY, J. f. Psychol. u. Neurol. **35**:283, 1928.

The study of the architectonic structure of this cortex in the dog is unusually difficult, because the borders of the various areas are indistinct and artificial. In addition to this, there is a great individual variability in the fields and in the depths of the fissures. The authors' measurements showed that almost 55 or 60 per cent of the dog's cortex is hidden in the depth of the fissures. A study of the nerve cells has also shown that most of these are unusually wide and rather plump; elongated and delicate cells are rare. It is also characteristic of the dog that the granules are large, the striking difference between the granules and the other nerve elements noted in primates is entire lacking in the dog. This fact adds another difficulty in the attempt to determine the presence or absence of the granular layer in any given field in this animal. Most of the cells take the usual stains poorly—this has already been emphasized by Brodmann. Another characteristic feature of the cortex of the dog is the presence of a peculiar type of cell in addition to the usual ganglion cell—it is a fine, elongated, frequently spindle-formed cell, with corkscrew-like protoplasmic prolongations and a small dark nucleus; this cell assumes an intense color with toluidin blue, and in contrast with the pale wide ganglion cells appears almost black. These cells are found in various numbers in the different areas. At first, the authors were inclined to regard them as pathologic and perhaps due to age or to disease; but they were found so consistently in apparently healthy animals that the authors are certain that they are a normal feature of the dog's cortex. Later, Economo found a similar type of cell in the limbic areas in man.

The paper is concluded with a detailed study in which the various areas are carefully mapped out, but which, for obvious reasons, cannot be reproduced in an abstract.

KESCHNER, New York.

A DIENCEPHALIC MECHANISM FOR THE EXPRESSION OF RAGE WITH SPECIAL REFERENCE TO THE SYMPATHETIC NERVOUS SYSTEM. P. BARD, Am. J. Physiol. **84**:490 (April) 1928.

Bard reports interesting data derived from acute ablation experiments on a series of forty-six dogs, which bear on the diencephalon as a seat of emotional control. After decortication the ether anesthesia was stopped and observations were recorded as successive slices were removed distad along the brain stem. The work was exceptionally carefully done, and the results seem unequivocal. It appears that typical sham rage becomes manifest on brain ablation up to the midpoint of the diencephalon and after removal also of the dorsal portion of the thalamus. That is, the area comprised by the caudal half of the hypothalamus, with the caudal and ventral-most portion of the corresponding thalamic segment, may be assumed to represent the controlling center for primitive emotional response, at least of the rage type. There is likewise ground for belief that in this area are structures important in the releasing of response of the sympathetic nervous system, as observed under circumstances of stress. This may be inferred from the marked sympathetic discharge noted as forming part of the sham rage picture, principally, erection of the tail hairs, toe pad sweating, retraction of the nictitating membranes, exophthalmos and striking elevation in blood pressure and heart rate. This contribution obviously is of considerable importance in respect to the problem of affect, both in normal relations and likewise in pathologic states, such as for example, hysteria, schizophrenia and epidemic encephalitis.

RAPHAEL, Detroit.

THE PROGNOSIS AND THE LATE RESULTS OF POSTENCEPHALITIC RESPIRATORY DISORDERS. W. ALDREN TURNER and MACDONALD CRITCHLEY, J. Neurol. & Psychopath. **8**:191 (Jan.) 1928.

The authors state that although the number of cases which form the basis of their article is too small to justify definitive conclusions as to prognosis, it is possible that the twenty-nine cases investigated constitute a representative example of postencephalitic respiratory disorders in general. Almost every variety of known breathing anomaly was represented. Nearly one half of the cases either have ceased to show any respiratory disorders or else have shown them to an attenuated extent. An equal proportion of cases remained unchanged over a period of time extending up to three years. Two patients died while still giving evidence of a respiratory disorder. It appears that the character of the breathing anomaly does not materially alter the prognosis. The proportion of cases in which there was recovery appears to be greater in the cases with a progressive parkinsonian state than in those without the manifestations of paralysis agitans. Certainly, numerous physical and psychic stimuli may temporarily influence the severity of the disorder, but there is no evidence that these factors are other than temporary. The recovery rate apparently does not depend on any particular treatment; improvement seems to come spontaneously.

FAVILL, Chicago.

THROMBOSIS OF THE CENTRAL ARTERY OF THE RETINA. H. VILLARD and C. DEJEAN, Ann. d'ocul. **165**:241 (April) 1928.

A case of so-called thrombosis of the central arteries of the retina is reported, and the authors discuss whether these lesions are really due to thrombosis or whether they are due to embolism. They maintain that the question is not yet settled, but state that the modern tendency is in favor of thrombosis as the probable cause. They refer to a case recently reported by Opin, the embolic nature of which can hardly be doubted because of the careful pathologic study. The authors believe, however, that all cases are not due to embolism, and that they are dissimilar both clinically and pathologically.

They report the case of a woman, aged 71, who was suffering from arteriosclerosis and hypertension, and had attacks of mild dimming of vision which became more frequent until there was absolute loss of sight. The ophthalmoscopic examination revealed marked constriction of the retinal vessels. Absolute glaucoma, necessitating enucleation, followed in three months. The clinical picture was not typical, as the blindness did not come on suddenly; the fundus did not present the usual milky, edematous appearance and the red spot of the macula was absent. Pathologic examination of the optic nerve showed advanced endarteritis of the central retinal artery which extended into a thrombus. It is concluded that the lesion in this case was a thrombus in the central artery and that careful study of the clinical symptoms, compared with the pathologic examination, is the only way to make a differential diagnosis between the two conditions.

BERENS, New York.

STUDIES ON THE OCCURRENCE OF EXTENSOR RIGIDITY IN MAMMALS AS A RESULT OF CORTICAL INJURY. N. B. LAUGHTON, Am. J. Physiol. **85**:78 (May) 1928.

The author's studies took the form of acute and chronic extirpation experiments on a well controlled series of mammalian subjects, including cats, dogs, rabbits and guinea-pigs. The latter two forms, it should be mentioned, were utilized only for foreleg observations because of the difficulty of eliciting lower limb responses by cortical stimulation in these animals. Laughton's results are briefly summarized as follows: One-sided ablation of the motor limb areas in cats and dogs is followed by extensor rigidity in the opposite legs; similar ablation of merely the upper limb area, in all four types of subjects, results in like response of the opposite foreleg. When one hind leg region is extirpated, extensor rigidity is noted in the heterolateral member, but one-sided removal of the area frontalis in cats was not followed by such result nor by homolateral paralysis. Homolateral

paralysis was observed subsequent to all leg area extirpations, but it persisted, however, over a distinctly shorter period than the contralateral rigidity phenomena. In these experiments both rigidity and paralysis were also more marked and lasted longer in the upper extremities than in the lower. The manifestations noted are thought to be representative of the "release" from cortical domination of the lower mechanisms mediating postural tone, and serve strongly to indicate the significance of the former in relation to the complete, all-level integration necessary for effecting skilled and purposive movement.

RAPHAEL, Detroit.

HOMONYMOUS HEMIANOPIA IN THE COURSE OF PREGNANCY. SCHIFF-WERTHEIMER, Ann. d'ocul. **165**:263 (April) 1928.

Two cases of homonymous hemianopia were observed by the author in pregnant women in whom the conditions were normal except for a slight lowering of blood pressure. The lesion is localized in the region of the cuneus and is supposed to involve the posterior cerebral artery or one of its branches. It is evident that the lesions in these cases were due to spasm of the arteries, but this does not explain the mechanism of the lesion nor does it throw light on the etiology. It is suggested that pregnancy modifies all the endocrine secretions, and this alteration in secretion may affect the sympathetic system.

HYPERTENSION OF EMOTIONAL ORIGIN IN THE CENTRAL ARTERY OF THE RETINA. M. J. DUBAR, Ann. d'ocul. **165**:263 (April) 1928.

The author has noted that emotion provoked by the sound of a falling object, by a loud cry or by means of firing a revolver behind the patient, causes a rapid rise in the tension in the central artery of the retina, the systolic pressure being more markedly affected than the diastolic. Bailliart, in discussion, points out the necessity of reassuring the patient before studying the pressure of the central retinal arteries, if one wishes to obtain accurate readings.

BERENS, New York.

ADAPTATION VERSUS EXPERIENCE AS AN EXPLANATION OF MODIFICATION IN CERTAIN TYPES OF BEHAVIOR (CIRCUS MOVEMENTS IN NOTONECTA). L. B. CLARK, J. Exper. Zool. **51**:37 (May 5) 1928.

Notonecta undulata with one eye covered usually performs circus movements in a beam of light. Circus movements are eliminated in a well defined beam of light if a number of trials are made or if the animal is merely exposed in the beam without making circus movements. After circus movements have been eliminated in a beam, this modification persists as long as the insect remains in the beam, but it disappears if the insect is subjected to darkness for some time. The time before circus movements are eliminated in a beam of light is correlated with the time and intensity of light of previous exposure. When one eye is dark-adapted and the other light-adapted, the insect performs circus movements toward the dark-adapted eye, but they are eventually eliminated. The elimination of circus movements is probably due to light adaptation rather than to experience. The process involved consists in light adaptation causing such a decrease in the sensitivity of the eye that illumination effective in causing circus movements falls below the threshold of stimulation.

WYMAN, Boston.

FAMILIAL FACIAL PALSY. M. REESE GATTMAN, J. A. M. A. **90**:1870 (June 9) 1928.

A case of central facial palsy in a woman, aged 29, is reported. Four years before the present illness she had awakened one morning with stiffness and difficulty in moving the right cheek; this had progressed up to the present condition. There had been no exposure to draft or cold, but she volunteered the information that the palsy was no great surprise as several relatives on the maternal side of the

family had been similarly affected. A study of the heredity was made with the following results: The maternal grandmother had facial palsy at 58. She had had three daughters and four sons; three of the boys and one girl had facial palsy at the ages of 17, 19, 44 and 51, respectively. One of the unaffected children was the patient's mother. All cases were of the central type. None of the living members gave a positive Wassermann reaction. The author offers no explanation, except coincidence, and the suggestion of an underlying central lesion is only conjectural.

CHAMBERS, Syracuse, N. Y.

NEW PHYSIOLOGIC FACTS CONCERNING THE OCULOPUPILLARY FIBERS OF THE CERVICAL SYMPHATHETIC. R. LERICHE and R. FONTAINE, Presse méd. **34**:1313 (Oct. 20) 1926.

From observations reported in several earlier papers, the writers conclude that some sympathetic fibers for the eye leave the cervical chain, immediately above the first thoracic ganglion, to follow the vessels. They then report a new case as follows: 1. Following excision of the superior cervical ganglion, ptosis on the side on which operation was performed became progressively worse and was practically complete after five weeks, except that it could always be momentarily and proportionately relieved by turning the head to one side. 2. Excision of a neuroma about the sympathetic chain relieved the ptosis immediately and almost completely, i. e., it reverted to that grade normally expected after section of the cervical sympathetic.

HUDDLESON, New York.

EMOTIONAL POLYCYTHEMIA. EDITORIAL, J. A. M. A. **90**:1875 (June 9) 1928.

In addition to the chronic form of excessive erythroblastic activity known as erythremia, there occurs an acute manifestation of increase in the red cells of the blood known as emotional polycythemia. In animals subjected to undue excitement, an increase of 25 per cent in the erythrocytes of the peripheral circulation has been noted. Ferrari has shown an increase of 457,000 erythrocytes in students following an examination. Such gains could be due to removal of plasma or to a discharge of cells into the blood stream from some reservoir. Recent work has shown the spleen to be the immediate cause of polycythemia.

CHAMBERS, Syracuse, N. Y.

THE ACETIC ANHYDRIDE TEST IN CEREBROSPINAL FLUID. J. G. GREENFIELD and E. ARNOLD CARMICHAEL, J. Neurol. & Psychopath. **7**:220 (Jan.) 1927.

A complete study, including the acetic anhydride test, was made of fifty spinal fluids. Reaction by the latter method cannot be associated with any single one of the usual syphilitic reactions, or with any known combination of these. It is possible to get a negative acetic anhydride reaction when there is an increase in cells and globulin, a general paralytic type of Lange curve, and a positive Wassermann reaction. Accordingly, it is only fair to assume that the causal factor of the reaction must be some substance in the fluid other than that producing the other reactions. The suggestion is made that it may be due to an increase in the cholesterol content of the fluid.

FAVILL, Chicago.

BILATERAL EMBOLISM OF THE CENTRAL RETINAL ARTERY. T. G. WYNNE PARRY, Brit. M. J. **1**:178 (Feb. 4) 1928.

A man, aged 74, suddenly developed blindness in the right eye and three months later in the left. There was no perception of light, the pupils were dilated, equal, regular and inactive. The right fundus showed a pallid, clear-edged disk; many of the vessels were obliterated and the remainder were threadlike. There was some faint brownish pigmentation at the macula. The left eye showed the typical picture of recent retinal embolism — the pale disk, the vessels diminished in caliber,

a general pallor of the fundus with the "cherry-red spot" at the macula. Embolism of the central retinal artery is practically always unilateral; in thirty-seven years only three bilateral cases were observed at the Tübingen eye clinic.

PETERSEN, Montreal.

A NEW PERIMETER. HENRI B. GROS, Ann. d'ocul. **165**:255 (April) 1928.

In this article the tangent screen is criticized, and the author points out that most careful studies of the visual field can be made on the inner surface of a half sphere. As the large perimeters, suggested by Walker and Gaudissart, are too large for the ordinary consulting room, Gros has constructed a perimeter made from an inverted beach umbrella placed on a stand and covered by a black cloth, on which are traced red and blue circles at intervals of 5 degrees. The apparatus is designed for use at 1 meter, and at this distance gives accurate readings.

BERENS, New York.

INDUCTION OF PREMATURE LABOUR IN RELATION TO MENTAL DISEASE. R. PERCY SMITH, Brit. M. J. **1**:9 (Jan. 7) 1928.

The author presents two groups of cases, seven in which pregnancy was allowed to continue and ten in which it was terminated before viability of the child. The first group shows how acute insanity may run its course during the whole of pregnancy and yet recovery may result. The mental condition of four of the patients improved during the pregnancy and before parturition. The author concludes that only purely medical considerations should be allowed to weigh in deciding as to the termination of pregnancy, and quotes several opinions in support of his belief.

THE PROPORTIONAL FREQUENCY OF GENERAL PARALYSIS OF THE INSANE AND LOCOMOTOR ATAXIA IN DIFFERENT SOCIAL GROUPS. PETER L. MCKINLAY, J. Hyg. **27**:174 (Jan.) 1928.

An examination of the statistics relating to broad groups of social classes in England and Wales as a whole suggests that general paralysis of the insane is proportionately more frequent among the lower than among the upper occupational classes. If, as is commonly believed, excess of mental work is a factor of importance in the etiology, its influence must therefore be more than counterbalanced by other more important predisposing factors, which must occur more frequently in the lower social classes.

PETERSEN, Montreal.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Jan. 19, 1928

HENRY R. VIETS, M.D., *President, in the Chair*

METASTATIC TUMOR IN THE FOOT OF THE LEFT THIRD FRONTAL CONVOLUTION, WITHOUT APHASIA. DR. PERCIVAL BAILEY.

S. G., aged 63, a Spanish laborer, was admitted to the Peter Bent Brigham Hospital, on Nov. 25, 1927, in the service of Dr. Harvey Cushing, having been referred by the Boston Psychopathic Hospital. Although he had been in the United States for thirty-eight years, he understood little English. The history was obtained by the aid of a Spanish nurse and coincided well with that obtained by Dr. Pardo of the Philippine Public Health Service at the Psychopathic Hospital. The patient had never been seriously ill. Possibly he had a chancre at the age of 26. When he was 16 he was accidentally shot in the right eye by an air rifle. The present illness began about Nov. 1, 1927, with headache in the occipital region. He was in New York City at this time and returned to Boston to remain with friends. Here he slowly developed a weakness of the right leg and was taken to the Haymarket Relief Station; from there he was transferred to the psychopathic ward of the Boston City Hospital and from there to the Boston Psychopathic Hospital where Dr. Macfie Campbell made a diagnosis of cerebral tumor. He was seen in consultation by Dr. Tracy Putnam who advised his admission to the Peter Bent Brigham Hospital. In the meantime, his right arm had become weak, and mental disturbances were marked.

Examination.—When the patient was admitted to the hospital he was restless, talked almost continuously and was irritable and suspicious. When he was addressed in his own language, however, he answered readily and rationally, though with evident loss of memory and at times with disorientation. A right hemiplegia was present mainly affecting the right leg, to a less extent the right arm, and leaving the face practically free. There was no spasticity, although the tendon reflexes of the right leg and arm were exaggerated. Bilateral choking of the optic disks, with hemorrhages in the left retina, was found. An x-ray picture of the head showed a lead shot in the right antrum. The patient was noisy and difficult to control.

Operation.—On Dec. 5, 1927, a left cerebral exploration was done by Dr. Horrax and Dr. Oljenick, and a nodule of tumor, apparently on the surface (recognized at the time as probably metastatic), was removed from "just above the large sylvian vessels at their anterior end." It measured about 3 cm. in diameter.

The body temperature rose to 102 F. and remained at about this level until death, on December 8, at 6:30 p. m. During this time, the patient was fairly quiet and practically comatose.

An x-ray picture of the chest, taken by Dr. Sosman on December 6, showed "old fractures of several ribs in the posterior portion of the left chest, healed and in good position. The left diaphragm is quite high in its medial third behind the heart, and there is a rounded soft tissue shadow in the outer portion of the right hilus. This may be a metastatic malignancy. The high diaphragm suggests the possibility of carcinoma of the stomach."

Postmortem Examination.—A necropsy was performed by Dr. Meagher six hours post mortem and disclosed: hypostatic bronchopneumonia, syphilitic aortitis, aneurysm of the aorta and primary carcinoma of the right lung with metastases in the liver, left kidney, both suprarenals and the brain.

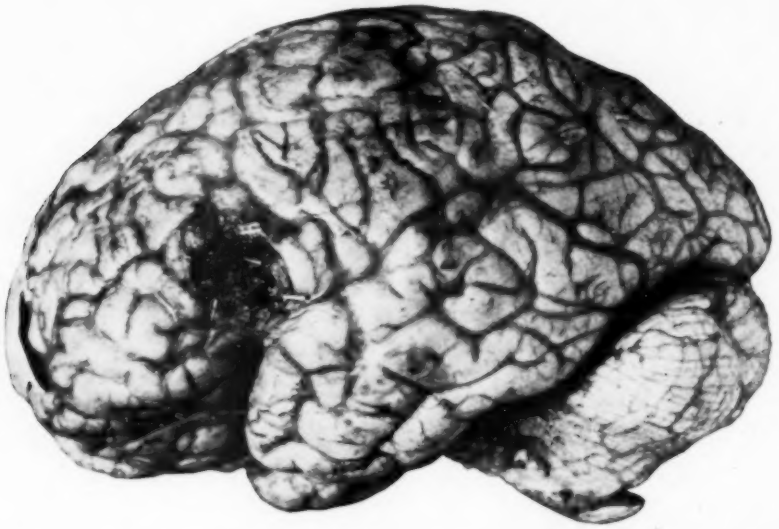

Fig. 1.—Defect in the left third frontal convolution after removal of the metastatic nodule of carcinoma.

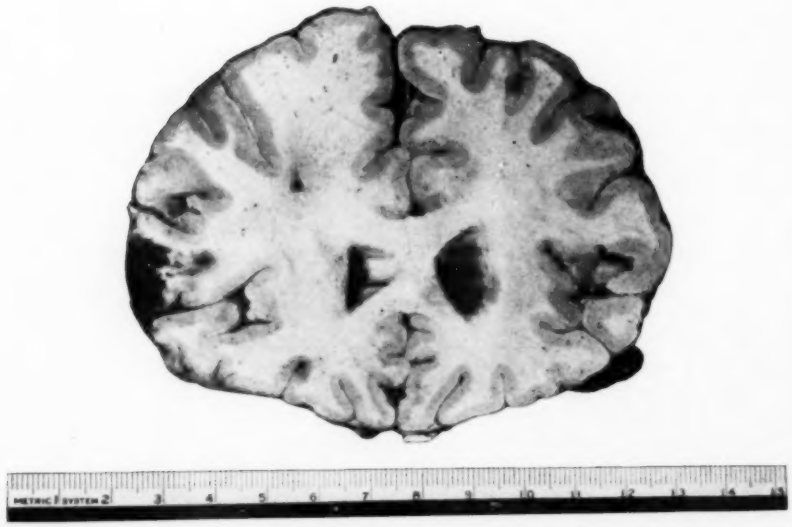

Fig. 2.—Transverse section of the brain shown in figure 1. The defect in the left third frontal gyrus should be noted.

It is the condition of the latter organ that is interesting. Before removal, the brain was injected with 10 per cent solution of liquor formaldehydi through the carotid arteries. On the surface a ragged defect could be seen, 1.5 cm. in diameter, exactly in the foot of the left third frontal convolution (fig. 1). This localization was confirmed by cross-section (fig. 2). There was also a nodule in the tip of the first left frontal convolution, another in the motor leg area of the left precentral gyrus and a third in the center of the cerebellum.

The nodule in the third frontal convolution is most interesting, for at no time was any evidence of aphasia noted by the patient's friends or by the various physicians and nurses who examined him. He talked to himself in a monotone almost constantly and if there had been any misuse of or difficulty in finding words it would certainly have been detected. He always answered questions addressed to him in his own language intelligently. At the Peter Bent Brigham Hospital there is no record of any attempt to get him to read, but he could do so when examined at the Psychopathic Hospital.

His friends affirmed that he was right-handed, and although there is no record that the patient was asked concerning the matter while in the hospital, there is no reason to doubt the testimony of his friends on this point.

It seems, therefore, that one is dealing here with a metastatic nodule in Broca's convolution, without aphasia. I have already pointed out the importance of metastatic tumor nodules in the study of aphasia and have described two cases which seem to confirm the ideas of Pierre Marie concerning the localization of lesions disturbing the function of speech (Bailey, Percival: A Contribution to the Study of Aphasia and Apraxia, ARCH. NEUROL & PSYCHIAT. **11**:501 [May] 1924). It is interesting to recall Marie's description of how Broca came to localize the function of speech in the third frontal convolution (Marie, Pierre: L'aphasie de 1861 à 1866. Essai de critique historique sur la genèse de la doctrine de Broca, *Semaine méd.*, Nov. 28, 1906).

(The case was then used as a text for an account of the work of Broca, as recorded by Pierre Marie.)

DISCUSSION

DR. C. MACFIE CAMPBELL: Was this patient right-handed or do you know whether he appeared to be right-handed in adult life? Was he right-handed as a child? Dr. Orton has shown how difficult it is to be sure that a patient is right-handed. I remember one case of aphasia in a paretic patient who at autopsy was found to have a lesion of the right hemisphere. When the history was investigated, it was found that as a child he had been trained, with a great deal of difficulty, to be right-handed.

BARRIER BETWEEN THE BLOOD AND THE CEREBROSPINAL FLUID. DR. WILLIAM MALAMUD, DR. DOUGLAS M. FUCHS and DR. NATHAN MALAMUD.

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DISCUSSION

DR. KARL M. BOWMAN: I shall stress two points: (1) The difficulty of diagnosis of such disorders as dementia praecox and manic-depressive psychoses. As far as I could follow Dr. Malamud, it seemed as if the readings in the manic-depressive group were all within normal limits, while those in the dementia praecox group were not. I wonder whether other clinics would give the same diagnoses as Dr. Malamud in these cases. There is so much divergence of opinion that I think one is entitled to raise this question. My opinion is that different clinics have different standards for making diagnoses and that that may be the explanation of why one of the German clinics, as Dr. Malamud reported, gave such different results from the rest of the clinics. (2) Dr. Malamud said that he disregards the concentration of bromide in the blood, or rather that he disregards it within certain limits. He did not state what these limits were, and it seems that unless they are extremely narrow they cannot be disregarded. If, as has been suggested,

bromides in the blood are combined with proteins, the exact amount of bromide present in the blood would be of the greatest importance, because if only a small amount were present it might be completely taken up by the proteins in the blood and there would be little or none to diffuse over into the cerebrospinal fluid. The fact that there are so many views as to how these different substances get from the blood into the spinal fluid should be kept in mind. It is well to remember that in the kidney, for example, there is a selective action in regard to sugars. There is a definite threshold at which dextrose passes from the blood into the urine, whereas other sugars, such as lactose and fructose, will pass through the kidney into the urine even if the smallest amount is present. If any such mechanism as this regulates the passage of substances from the blood into the cerebrospinal fluid, it must be apparent at once that the concentration of bromides in the blood would be of great significance.

DR. WILLIAM MALAMUD: In the light of recent investigations of the nature of the cerebrospinal fluid, one cannot speak of this blood-cerebrospinal fluid barrier simply as a semipermeable membrane. The nature of it is probably much more complicated, and its localization may have to be looked for in some constituent of the plasma which fixes part of the bromides and which varies with different diseases. This, however, would not alter the concept of the barrier, but would simply shift its localization and throw new light on its nature. A great deal more work is necessary, however, before one can come to a solution of this part of the problem. I agree with Dr. Bowman that some of the diagnoses in the field of psychiatry are not as reliable as in other fields. So, for instance, the borderlines between manic-depressive psychoses and schizophrenia vary to a certain extent in different institutions. I do think, however, that even in the case of these two disease entities, all agree on a certain typical syndrome and may disagree only in questionable cases. In most of the other disease entities, this divergence of opinion is even less as one has more reliable criteria to go by. When such criteria are not yet established this work along with others of its type may serve as a starting point. As to the second question, I will repeat that Walter, in his communications, stated that he did not find any relation between the absolute blood content (unless it was too low) and the permeability index. Our determinations varied between 1 : 2,000 and 1 : 6,000, the average (most of the cases) being 1 : 4,000. Repeated determinations on the same patients with different blood contents did not show an appreciable difference in the permeability quotient. I have not had experience with cases in which the patient showed a high temperature during the determination of the permeability. Other authors report increased permeability in meningitides. In my experience, a chronic inflammatory process (e. g., paresis) goes with an increased permeability. The suggestion that some treated paretic patients may develop paranoid ideas concomitantly with decreased permeability is partly substantiated by the reports of some European investigators of the malarial treatment for paresis. Kirschbaum, for instance, found the development of paranoid ideas in some of his cases. He has not undertaken determinations of permeability, however. In my material, I have not found any such cases.

Regular Meeting, Feb. 16, 1928

HENRY R. VIETS, M.D., *President, in the Chair*

VOLUNTARY DISSOCIATED MOVEMENTS OF THE EYES. DR. JAMES B. AYER.

Moving pictures were shown of two brothers, aged 18 and 25 years, respectively. Both had normal vision and under usual conditions presented normal movements of the eyes. One was a student of medicine, and the other was in college; both were in good standing.

In each case a certain voluntary control over the ocular muscles had been acquired, and analysis appeared to show the same ability of monocular control,

although differing in degree. With the eyes held rigidly in convergence, one eye was maintained in this position while the other moved slowly outward and back again to the position of convergence. In both subjects, monocular movement was possible in either eye. In the younger boy, particularly, the movement of the eye was wide, even to the outer canthus, and the control of movement was good.

The question was raised as to the nature of the movement. Was the phenomenon one of monocular relaxation with the other eye in the primary position of convergence, or was there true voluntary motion perhaps due to separate ocular muscle cortical representation?

DISCUSSION

DR. E. W. TAYLOR: It would be interesting to know how far this could be cultivated in other normal persons. It would also be interesting to know whether these particular men have the power of moving other muscles; for instance, the muscles of the ears, or others not ordinarily under control of the will. I am inclined to think that if we had all set about doing this in our younger days we might have accomplished the same results.

A PHYSIOLOGIC THEORY OF STREPHOSYMBOLIA AND STUTTERING IN CHILDREN. DR. SAMUEL T. ORTON, Columbus, Ohio.

The term strephosymbolia is used to include cases of typical "word blindness" and also the demonstrably much larger group of children who are retarded in reading much below their achievement in other subjects (notably arithmetic) and whose attempts at reading are characterized by frequent reversals in reading, by confusion between reversible words and who show a greater facility in mirror reading than do normal readers.

Understanding of the spoken word, reading, speech and writing are all under the unilateral control of the dominant hemisphere. Visual stimuli are, however, bilaterally implanted both at the first or perceptual level and at the second level of functional elaboration where the meaning of objects is added to perception. Only at the third level, that is, in the language zone, does unilateral dominance appear. Notwithstanding the striking difference in functional importance of the two hemispheres at this level there is little if any structural difference, and to account for this equality in growth one must assume that both sides have received an equivalent irradiation and further that the nondominant hemisphere must therefore retain records or engrams of such irradiation. Under this envisagement the establishment of dominance would appear to consist of the acquisition of a physiologic habit for the exclusive use of the engrams of the dominant side, and this assumes the elision of those of the nondominant. When this habit is not adequately acquired, conflict in lead between the antitropic engrams of the two hemispheres would result, and I feel that this is the explanation of the confusions, reversals and mirror reading which characterize the retarded readers. Our extended observations covering 175 retarded readers seem clearly to establish the belief that strephosymbolia constitutes a clinical entity which is not related to mental defect and which responds quickly to special retraining methods based on the physiologic theory. I now believe that in even the most severe cases the patients can be taught to read if proper measures are instituted early and carried out consistently.

The speech mechanism also is controlled from the dominant hemisphere and apparently the complex integrations which constitute orderly speech are a unilateral function of the language zone. In the stutterer's efforts at speech, there is evidence of striking disintegration of the various reflex units employed. The frequent association of stuttering with an enforced change in handedness, in writing especially, and certain of our observations on the action current patterns of the two forearms support the suggestion that stuttering also is due to a confusion in cerebral dominance. My theory is not as concise here as in strephosymbolia and the series of cases is not so large, but some of the retraining experiments are highly promising.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, Feb. 16, 1928

DR. JOHN FAVILL, *President, in the Chair*

COMPLETE FACIAL PARALYSIS. DR. LOYAL DAVIS.

Dr. Davis presented a patient who had complete facial paralysis, as the result of an embryonic tumor mass, for which a spinal accessory anastomosis had been performed.

THALAMIC SOFTENING. DR. HARRY A. PASKIND.

Dr. Paskind presented a patient with involvement of the sensory distribution of the right trigeminal nerve, due to "thalamic softening."

History.—This man, aged 70, a salesman, a patient of Dr. Patrick, was first seen on Jan. 17, 1928. The family history was unimportant except that an elder daughter, aged 40, at 18 experienced loss in hearing without pain or suppuration, and the condition had been slowly getting worse. At the age of 20, the patient began gradually to lose hearing without aural pain or suppuration; this had been gradually and slowly growing worse. At the time of presentation he could not hear at all on the left and only poorly on the right. About twelve years before the present illness, he first noticed a cold heavy feeling in the ball of the left foot; this gradually spread, and in six months involved the entire left leg; this feeling has remained stationary. A week after the onset of this condition, he noticed flexion contraction of the first three toes of the left foot; this also remained unchanged. Pain in these toes was elicited on walking, but there was none when the patient was at rest.

About twelve days before he was first seen, the patient was exposed to a draft. Two days later, in the evening, he noticed a dull pain around the right eye which has been present since. The next morning, on awakening, he rubbed the painful region and noticed that his forehead on the right side was numb. At the same time, he felt a sensation of "pins and needles" over the right malar prominence. The numbness and painful paresthesia, or dysesthesia, spread and in two days involved the entire right half of the face, the right edge of the tongue, the right upper gum and the right frontal region to the vertex; in other words, the sensory distribution of the right trigeminus. There were no severe jabs of pain, but the painful "pins and needles" sensation had kept him awake for the preceding two nights. The sensation was worse when he was talking. At the onset there were no speech difficulties, dizziness or weakness in the arms or legs.

Examination.—The right ankle reflex was distinctly greater than the left. The right knee reflex was slightly greater than the left. The right biceps reflex was greater than the left; otherwise, the arm reflexes were normal. The plantar, abdominal and cremasteric reflexes were normal. The pupils were normal. The visual fields were grossly normal. There was slight tactile anesthesia of the right side of the face, but no thermanesthesia. Although he complained that the right side of the face, and especially the right frontal region, was numb, it was hyperalgesic, i. e., pinpricks caused more distress on the right. The motor function of the trigeminus was normal. Perspiration was freer on the left than on the right side of the face. The blood pressure was 118 systolic and 85 diastolic. The pulse in the feet was faint, but palpable. There was marked ankylosis of the first interphalangeal joints of the second and third toes of the left foot.

Course.—During the night following the first visit, the patient experienced excruciating pain for four hours in the right side of the head from the hair line to the vertex. The condition was diagnosed by Dr. Patrick as one of thalamic softening; thrombosis in the thalamus.

I saw the patient again this morning. Numbness and dysesthesia have been present continuously; in the last few days the condition has been getting worse.

When he was examined this morning, it was found that oversensitiveness to pin prick was absent in the right side of the face; he was less sensitive to prick in this region, but oversensitiveness to pricking was still present in the frontal region. He was extremely oversensitive to pressure and pinching in the right side of the face. This morning, also, he showed slight thermanesthesia in addition to slight tactile anesthesia of the right side of the face.

The thalamic syndrome was first described by Dejerine and his pupils, Roussy and Thomas, in 1903. The syndrome need not be complete, however, as this case demonstrates.

In 1912, Head and Holmes studied such cases and demonstrated the presence of a tendency to overreact to unpleasant stimuli in the affected regions, and they considered this overreaction diagnostic for thalamic lesions. Head believed that central pain was caused almost entirely by thalamic lesions. That is, he stated that he had never observed central pain except in lesions of the thalamus, and he thought that only a few of the reported cases of lesions below the optic thalamus causing central pain would stand criticism. Head also believed that central pain, painful paresthesia and overreaction to unpleasant stimuli in an area showing sensory loss, represented a loss of cortical inhibition.

These views have been contested especially by Weisenburg and Stack, and by Spiller. The former, in 1923, cited several cases from the literature and two cases of their own in an attempt to prove that central pain may result from lesions of the sensory fibers in any portion of their intramedullary course from the spinal cord to the cortex, providing the lesion is such as to irritate the fibers and not to block conduction through them. Spiller, in 1923, described oversensitiveness to unpleasant stimuli in areas showing sensory loss in syringomyelia, in lesions of the medulla and in a lesion presumably of the pons.

Oversensitiveness in areas with sensory loss is a wise provision, for it forces the animal to withdraw the stricken area from noxious stimuli. This reaction is of so much value to the organism that it may well arise in lesions of the central sensory tracts other than those of the relatively small part of this system represented by the thalamus. In view of this, it is understandable that Weisenburg and Stack, and Spiller found this anomalous reaction in lesions of the intramedullary sensory system apart from the thalamus.

TRIGEMINAL NEURALGIC PAIN ASSOCIATED WITH MULTIPLE SCLEROSIS. DR. HARRY L. PARKER.

Severe protracted pain in cases of multiple sclerosis is so rare that it seems hardly worthy of discussion. However, during the course of nine years and in a long series of cases of multiple sclerosis, four cases were noted in which the patients complained bitterly of intense paroxysmal neuralgic pain, localized in one or more divisions of the fifth nerve. To these patients pain seemed to be the most important complaint of their disease, and they demanded relief, regardless of what else could be done to ameliorate the other symptoms. Accordingly, these cases stand out in bold relief from the general run of cases of multiple sclerosis and, as such, demand some inquiry.

The first patient had had obvious signs of multiple sclerosis for twenty years and at the time of examination all symptoms were well marked. He had had paroxysmal, trigeminal pain for six years in the second divisional area of the left fifth nerve. The type of pain of which the patient complained was identical with that in major trigeminal neuralgia. There were no objective signs of disease in the nerve. To relieve the pain, section of the posterior root was performed, with freedom from pain for four days preceeding death. A necropsy was performed and serial sections of the brain stem were stained with Weigert's myelin-sheath stain. Multiple sclerotic plaques were scattered throughout the brain stem. In the lower medulla, a plaque was found in the spinal root and nucleus of the fifth nerve on the right side. This disappeared at a level corresponding to the upper third of the inferior olivary nucleus. In the pons, opposite the main sensory

nucleus of the fifth nerve on the right side, there was a tonguelike projection of a large plaque which occupied nearly the whole length and breadth of the floor of the fourth ventricle. This plaque enveloped the sensory nucleus of the right fifth nerve. Both roots of the fifth nerve were traced upward in their oblique, outward course within the pons; they merged in the usual manner and formed the posterior root of the nerve. As traced upward, each root took the myelin stain well and did not seem degenerated, but just at the point of emergence of the left root two plaques appeared and engulfed its fibers. On the right side, the root seemed normal. Study of the left root in its extrapontile course showed that the sclerotic process extended outward a short distance within its substance when the root became seemingly normal again up to the point of its severance by the surgeon, where it was surrounded by a blood clot. Study of the left gasserian ganglion with various stains showed nothing more than could be attributed directly to the trauma of surgical intervention. The right gasserian ganglion and corresponding posterior nerve root were normal in all respects. Studies of the midbrain showed relatively few plaques, and the mesencephalic root of the fifth nerve on each side was apparently normal. The cerebellum was comparatively free, except for one large plaque, about 2 mm. in diameter, in its white matter near the nucleus dentatus and roof of the fourth ventricle. In the white matter of the cerebrum, there were many small, isolated plaques, and lining the walls of the ventricles large confluent areas of sclerosis were noted. The histologic appearance of the lesions throughout the nervous system was characteristic of multiple sclerosis.

The clinical history and observations of three other patients were similar in many respects to those of the patient just described. In all three, the posterior root of the fifth nerve on the side affected had been sectioned. Complete relief from pain was obtained in each case; this has lasted to date, without any change in the progress of the causal disease.

The four cases presented many similarities both in the course of the disease and in its salient features. In each the disease was so well established that three of the four patients had had symptoms for twenty, nineteen and thirteen years, respectively. The disease had begun in early adult life. In the remaining case the onset had occurred at least five years prior to operation. In all, the diagnosis of multiple sclerosis was established beyond any reasonable doubt. Two of the patients were observed over a period of years during the course of the disease. In all four the course had been the usual one of remissions and exacerbations. Necropsy was possible in one case in which the patient died after the operation; the conditions noted in the central nervous system after death were in accord with the previous clinical diagnosis of multiple sclerosis.

The pain syndrome in all four cases was identical; without exception it followed the course of major trigeminal neuralgia with the usual remissions and exacerbations. In three of the cases the pain was unilateral, in one both sides were affected. In case 4, the three divisional areas were affected: in cases 1 and 3, the second and third divisions were affected, and in case 2 the second division alone. In the cases in which more than one division was affected the pain had commenced in the second or third division and spread to the other in the course of time. Sleep was not greatly disturbed, but the patients dreaded the periods of activity enjoined by their daily needs and preferred to remain immobile lest an agonizing paroxysm should be initiated. Periods of freedom from pain were common, but they grew progressively shorter, and the patients were ready to accept section of the posterior root of the fifth nerve as a source of palliative relief, even though it did not bring hope of cure of other complaints.

The relation of the period of pain to the whole course of the disease varied in the four cases; two patients, who had had symptoms of multiple sclerosis for nearly twenty years, had suffered from pain only in the last few years. Two patients had had pain almost from the onset of the disease. One of the latter had had symptoms of multiple sclerosis for fourteen years and during twelve of these had suffered recurring attacks of paroxysmal trigeminal pain.

The resemblance of the pain syndrome in these cases to that in tic douloureux led to the same surgical measures being advised. So far as relief from pain is concerned, the operations were uniformly successful, since the three surviving patients have been free from pain to the present time, representing periods of two, six and seven years, respectively. Injection of alcohol into the nerve afforded temporary relief in a few instances but to a much less degree.

Discussion of the site and mechanism of the pain can be only speculative. It is manifestly impossible to form definite conclusions, since there are many possibilities of error. I have demonstrated, therefore, only the objective data; my interpretation of these data should be accepted in the spirit in which it is offered. The observations may be of some interest to those concerned in the problem of the causation of pain in general, and of that referred to the fifth nerve in particular.

DISCUSSION

DR. PETER BASSOE: I recall a woman patient, aged 37, who has had multiple sclerosis for seven years and typical trigeminal neuralgia for two years. I injected alcohol, with good result. I regarded it merely as a coincidence, and while Dr. Parker was speaking, I thought that it was only coincident in relation with the large amount of material at the Mayo Clinic; on seeing the sections, however, it certainly looked as if the condition of the fifth root might have caused the pain. Would the cutting off of all impulses explain the relief from injection of alcohol on the grounds that it requires peripheral stimuli to activate the pain? Dr. Parker certainly gave an excellent demonstration of an unusual combination of symptoms.

DR. FREDERICK HILLER: I remember one patient with definite multiple sclerosis whom I saw in Munich. He had symptoms of trifacial neuralgia. We did not wish to operate and so applied roentgenotherapy; this resulted in transient relief from symptoms. There was recurrence of pain; the patient died, and at autopsy a focus was found in the fifth root on the same side. This focus may have been a sufficient explanation for the pain. The question as to how operation could bring relief from the pain is interesting. The only explanation I could offer would be that cutting the sensory root of the fifth nerve may lead to degeneration of the sensory cells in the medulla oblongata. Did Dr. Parker find the nerve cells involved?

DR. LEWIS J. POLLOCK: In lesions of a peripheral nerve, the only pain encountered occurs in cases in which there is only partial injury. This is seen in causalgia and runs a characteristic course. Pain never occurs until about three weeks after the injury, at which time some motion returns. I have never observed severe pain in a case in which the nerve was completely sectioned. It is possible that when some sensory function is preserved pain may be elicited by some peripheral stimuli.

DR. G. B. HASSIN: If the patches are to be held responsible for the pain in Dr. Parker's cases, would not sensory phenomena in multiple sclerosis be as frequent and as marked as the motor? Many cases of multiple sclerosis show mild or no sensory disturbances, notwithstanding the fact that patches are found in the sensory pathways. The posterior roots, for instance, may be found to contain patches without corresponding disturbances of sensory function. I think Dr. Parker is right in hesitating to consider the pain as due to multiple sclerosis only.

DR. JOHN FAVILL: Does Dr. Parker know the total number of patients with multiple sclerosis seen during the period in which these four cases occurred? This might be of value in judging the possibility of coincidence.

DR. PARKER: The chief interest I had in this subject was in regard to the production of pain, especially of the type one observes in trigeminal neuralgia. I think no one is certain where the lesion in the latter disease is located. A number of pathologic studies have been made, but the observations have not been consistent. I thought that going over this material might give some hint as to the mechanism that produces this type of pain. Unfortunately, the problem still remains unsolved. The patients were relieved by section of the root, just as they are relieved in

trigeminal neuralgia. This does not, in my opinion, however, exclude the possibility that the pain is central to the part sectioned. I should be inclined to regard favorably Dr. Bassoe's suggestion that section of the root puts the peripheral part at rest; it stops further propagation of stimuli over the tract.

Replying to Dr. Hiller, I examined the sensory nucleus with Nissl stain, but did not find any definite changes. The patient, however, died shortly after the operation.

Regarding Dr. Pollock's remarks, I made out definitely that sensory or motor changes were not found in these cases before operation. This links up with what Dr. Pollock has said, that spontaneous pain is not usually present with complete analgesia. These patients had normal sensibility in the area of the fifth nerve, and in this respect differed somewhat from those patients who experienced central pain due to syringomyelia and tumors in the brain stem. My impression was that the pain was not due to a central lesion, but possibly to involvement of the sensory root at its entrance zone into the brain stem.

Dr. Hassin, I think, misunderstood me. My conclusion was that in these cases multiple sclerosis and the trigeminal pain were associated in some way. This is a matter of opinion, but other cases have been published in support of this assumption.

Dr. Favill asked the number of cases of multiple sclerosis seen at the Mayo Clinic. I did not make a statistical study. It would have had to be based on the assumption that in each case a correct diagnosis had been made, which would bring up the question of how much is included in the term multiple sclerosis. In the few cases presented the patients were carefully examined; clinically, they corresponded to that which is termed multiple sclerosis, but before making comparisons in large numbers a better understanding of what the term means is required.

DR. H. DOUGLAS SINGER: One kind of association does not appear to have been mentioned; both the multiple sclerosis and the pain might be due to a common cause, rather than one being due to the other.

DR. PARKER: Replying to Dr. Singer's remark, Dr. Hassin said that there are numerous changes in the sensory sphere in multiple sclerosis, but few objective changes. I think you will admit that objective changes are not common, while it is common to have subjective changes. In these cases, there were marked subjective changes but no objective changes.

MYELOGRAPHIC STUDIES OF THE SPINAL CANAL. DR. HANS REESE.

Myelography, or the injection of iodized oil 40 per cent into the subarachnoid space, was introduced by Sicard and Forestier in 1922. Since that time this method has been studied and applied in many clinics in this country as well as abroad. Its use in the early diagnosis of compression of the cord has been enthusiastically praised, but, on the other hand, many warnings have been heard.

At the University of Wisconsin, in the department of neuropsychiatry, the first use made of iodized oil was to confirm the diagnosis of lesions which were localized by means of neurologic and radiologic data. Later, we became convinced that to obtain the maximum information it was necessary to study the oil distribution in a large series of cases in which the pathologic process was not known. These observations gave information on normal distribution through the spinal canal, and the deposit in the region of the cauda equina. It is important to interpret properly partial or complete blocking of the descending oil, as well as the shape and distribution of the oil at the site of blocking.

Iodized oil has been used in bronchiectasis, in pleural exudations, and in tuberculous ascites, and may be used in an effort to modify pathologic reactions of the meninges. Injections of from 1.0 to 2.0 cc. of iodipin 40 per cent into the subarachnoid space in cases in which the meninges may be considered as normal produces, several hours later, drawing sensations in the lower extremities; these

sensations last about two days. If one injects the same amount in cases of spinal meningovascular syphilis or tabes, the procedure is followed by true crises of lancinating pain with disorders of the rectum and bladder that last from eight to twenty days. In such cases, the spinal fluid shows an increase in the number of cells and of the globulin content. The subjective complaints later become less severe.

This report deals with results obtained by injecting iodized oil into the subarachnoid cavity: (1) to outline the upper pole of obstructions; and (2) to demonstrate the lower pole of the obstruction by making a second injection of oil into the lumbar region while the patient is placed in Trendelenburg's position.

Clinical neurologic methods do not always determine the exact location and extent of an obstruction in the spinal canal. Deformities of the vertebral bodies, extradural or intradural hematomas, pachymeningitis, leptomeningitis, as well as the different tumors of the cord and its appendages, may produce incomplete blocking of the subarachnoid space with variable clinical observations. The x-ray pictures and serology may be normal. The symptoms of such obstructions are often vague, and it takes a long time for them to develop.

Sicard and others stated that iodized oil is harmless and does not irritate or damage the nerve tissue, the meninges or the nerve roots. Peiper, in Germany, studied the anatomic, physiologic and pathologic conditions of an iodized oil called iodipin on the spinal cord and meninges in a large series of rabbits. For obvious reasons such a study should have preceded the clinical use of the iodized oils in man. The oil is deposited in an almost immovable manner in a closed, delicate system; moreover, it is slowly absorbed by the organism. Peiper found that the ganglion cells of the anterior horns were especially affected; they showed chromatolysis and swelling with achromatosis. The cells of the posterior horns, on the other hand, were unchanged. His pathologic observations were similar to those following destruction of the axis cylinder from nerve intoxications or following lesions of the peripheral nerves. Apart from these changes of the motor ganglion cells, Peiper found some degeneration of the fiber tracts on the surface of the cord, without definite selection of particular tracts; after several weeks, Marchi's degeneration of the posterior columns took place from the lumbar region upward. These pathologic changes must be produced by absorption of the iodized oil through the lymph vessels. The pathologic changes, as seen in animals after intra-arachnoid injections of iodized oil, may develop in human beings, although they have not been reported as yet. They were absent in the following case:

A patient with an extramedullary tumor died of pyelocystitis six weeks after an injection of oil. There had been an absolute oil blockage at the seventh thoracic vertebra, which was confirmed by a successful operation. Postmortem examination of the cord failed to reveal any pathologic process or adhesions at the point where the iodipin had previously been arrested.

In the work at Madison iodipin 40 per cent has been used. Experience there was based on thirty-eight cases, of which six were extramedullary tumors, four adhesive meningitis, eight were compression myelitis, two were spina bifida, one was circumscribed cervical cyst and seventeen were lesions of the spinal cord in which the differential diagnosis lay between tumor, myelitis with adhesion, leptomeningitis and multiple sclerosis. In most of the cases, both cisternal and lumbar punctures were made, with examination of the spinal fluid and use of the Queckenstedt compression phenomenon. After an interval of one week, iodipin 40 per cent was injected.

Normally, after injection the oil reaches the cauda equina in two minutes. If there is an obstruction in the spinal canal, the oil will be partially or completely arrested. The first x-ray film is made five minutes after the puncture, while the patient is lying with head and shoulders slightly elevated, and should include the entire spinal column from a ventrodorsal and lateral view. If the iodipin is found in the cauda equina in the first picture, one may conclude that there is no obstruction. If, on the other hand, all the iodipin is not in the cauda equina at

the time of the first picture, it is necessary to make a series of exposures covering the entire length of the spinal canal. Large pearls of iodipin may be temporarily arrested; if these disappear on the second day a pathologic significance is not indicated. On the other hand, if the iodipin is permanently arrested, even after several days, one is justified in assuming the existence of a pathologic process, and surgical intervention should be seriously considered even in the absence of localizing neurologic symptoms. Temporary arrest of iodipin around the location of the injection as well as one or two small pearls in the spinal canal is of no significance. Sometimes, small droplets of oil are permanently arrested on both sides of the spinal cord; Sicard explained this as being due to calcification of the dura. The iodipin on its way downward is not always in one continuous mass; the oil may form on both sides of the cord, either in chains of oil pearls or as linear streaks of oil with small oil droplets following the exit of the spinal nerves through the meninges.

Complete blocking of the spinal canal produces a dense shadow which is convex along its upper border, with typical arms extending downward on both sides. Such a complete shadow has to be studied carefully, particularly at the sides. If these converge toward the obstruction it means an approach of the anterior and posterior dura over the obstacle; if they diverge it means a broad tumor which extends to the dural layers. Cases of chronic pachymeningitis or of meningeal adhesions show irregularities in the x-ray shadow and permanent accumulations of oil caught in adhesions at various levels of the diseased area. Depending on the strength of the connective tissues of the caudal sac, which is at the level of the second sacral vertebra, the heavy oil will cast a globular or a true conical shadow, with oil radiating into the dural sheaths of the sacral nerves. At present we are still unable to differentiate between extramedullary and intramedullary tumors even with x-ray exposures from different angles, and we have great difficulties in the interpretation of tumors of the cauda equina.

Besides the recognition of tumors and meningeal adhesions, injections of oil should be used in the differential diagnosis of vertebral fractures with or without compression of the cord. The oil silhouette will answer the question which otherwise could not have been answered without an exploratory laminectomy.

Irritations after injections of oil are only transitory, and consist of headache, slight meningism and rise of temperature on the second day without increase of the pulse rate. After the injection, we have observed a great increase in the globulins and cells, the pleocytosis in some cases rising to several hundred cells. All irritating symptoms disappear after from three to four days. Iodipin at the level of arrest above an obstruction in the subarachnoid space may produce severe root pains, which can be relieved by acetylsalicylic acid or morphine.

The oil remains for a long time in the subarachnoid space and in the cauda equina. It is absorbed by the lymph vessels after it has been saponified into a whitish substance by the alkaline spinal fluid. I have never observed disturbing effects from the deposited iodipin, except in cases of syphilis of the central nervous system.

In conclusion, I will state that myelography should be used only in cases of which a careful history and repeated neurologic examinations fail to explain the symptoms. Myelography should be used in all cases in which there are symptoms of persistent radiating neuralgia or neuritis, dull pain around a certain vertebral body with spasms of the long muscles of the back, incurable sciatica, and disorders of the bladder and rectum. The use of myelography should be restricted to cases in which absence of a distinct sensory level, absence of atrophy and paralysis, or reflex anomalies makes the differentiation between a tumor of the spinal cord, cyst, myelitis or adhesions impossible. Myelography permits more accurate and exact location of obstructions in the spinal canal than any other clinical procedure now known. It is particularly helpful to the surgeon at the time of operation, when the visualization of oil in the operative field gives complete orientation. Incidentally, the oil should be removed at this time.

DISCUSSION

DR. HILLER: I agree fully with the statements of Dr. Reese, but wish to mention that there is one contraindication to the use of iodipin in this manner. One patient I have observed had severe iodism afterward; the child had a severe dermatitis for a year after the procedure.

DR. DAVIS: Has Dr. Reese or his co-workers had occasion to operate on patients for the removal of the iodidized oil which had become encysted and caused symptoms similar to a tumor? Several instances have been reported in which this occurred, the pseudotumor mass causing the symptoms. I believe it is very difficult to remove the iodized oil from the subarachnoid space by operation. The tremendous reaction that one gets from the use of iodized oil should be emphasized, particularly the rise in globulin content and in the cell count.

In how many of the cases in which myelographic studies were made was it proved that tumors of the spinal cord were present?

DR. PARKER: We live in an era of haste, when the desire to reach an end in the quickest possible time is dominant. When the use of iodized oil was introduced, it seemed that a neurologist would no longer be needed. I think that the most valuable part of this paper was the demonstration that, with all these new methods of localization of the cord, there are certain fallacies and certain mistakes and that, instead of this being a quick method, there are many complications that one has to consider. One may misinterpret some of the results after injection of iodized oil and have to start all over again. I think the method should be kept in the background until all other methods, including the Queckenstedt test and a period of careful observation, have been proved ineffective. Then, possibly, in a certain number of cases, one can use this method. It has its disadvantages and is by no means the accurate and quick method of diagnosis one had hoped it would be.

DR. GEORGE W. HALL: Obstacles may arise in injecting the solution and placing the patient in the Trendelenberg position. Within the last ten days, Dr. Favill and I made a lumbar puncture and did not obtain any fluid; we were not sure that the needle was in the canal and did not wish to inject any iodized oil. A laminectomy was performed because the tumor appeared to be accurately localized; the Beevor sign was present and there was a rather accurate upper line of anesthesia. Operation revealed spinal fluid in good quantity above the tumor; below the tumor there was a gelatinous mass which could not flow through the needle when the lumbar puncture was made. In two or three other cases that I recall, the fluid was so coagulable that one was sure that there was a tumor. The blood had been found normal, but I thought it well to submit this gelatinous fluid to test; it gave a positive Wassermann reaction. Antisyphilitic treatment relieved the condition promptly, although the patient had entered the hospital with complete paralysis of both lower extremities.

I wish to compliment Dr. Reese on his conclusions; he was conservative in his statements, as he should be. It seems to me that iodized oil and other solutions of iodine have been much abused in the vast majority of cases; if one can study the patient thoroughly, one can arrive at definite conclusions without employing these preparations.

DR. BASSOE: Will Dr. Reese tell us what has become of "ascending" injection of iodized oil? When Sicard first brought out this procedure he used two oils, one light and one heavy; Dr. Reese used the same oil for both cisternal and lumbar injections. I presume that means that the light oil was not dense enough to give a good picture.

DR. REESE: Dr. Hall mentioned that syphilis may produce complete spinal blockage. I said that before I apply injections of iodized oil I examine the blood and the spinal fluid obtained by the cisternal and lumbar routes. I have published two cases in which the cisternal fluid examination gave negative results while the lumbar fluid gave a ++++ Wassermann reaction.

In a few cases, I have tried the ascending oil to which Dr. Bassoe referred, but the density is not great enough to obtain distinct shadows in the x-ray films.

Furthermore, it may be possible that it enters the ventricular system and produces ependymitis with blockage of the ventricular passages.

In two cases which I reported, there were symptoms of girdle constriction and segmental hyperesthesia and I felt justified in submitting the patients to an injection of iodipin 40 per cent; even with myelography, the diagnosis of complete blockage was not confirmed. These patients must have had adhesions in the posterior root system following myelitis, circumscribed chronic meningitis or multiple sclerosis.

Concerning the occurrence of iodism after the use of iodized oil, I examine the patient carefully for symptoms of hyperthyroidism and test his susceptibility by giving large doses of potassium iodide for a few days before the oil is injected. I have not seen cases of iodism.

In reply to Dr. Davis, it is true that it is difficult to remove all the oil or to tell during the operation that all oil has been removed, but if the oil reaches the caudal sac, it does not produce damage. I have not seen any encysted deposits of iodized oil in my cases. Animal experimentation with iodized oil can be done in rabbits, as they can be punctured easily by the cisternal route. One must start by injecting 0.05 cc. of a 10 per cent solution of iodized oil. Even when such a small amount is injected into the cisterna and the rabbit is held by the ears for a time, one cannot say with certainty that the alterations of the cord are not due to the trauma from the oil.

The series I reported did not include the cases in which we failed to diagnose a tumor of the spinal cord, as it did not occur to us that a tumor was present. In four advanced cases the observations pointed to a circumscribed meningomyelitis and we did not perform an oil injection.

Dr. Parker is correct. The cases are studied for several weeks, but if all known neurologic methods fail to lead to an exact diagnosis, then we use the myelography.

Regular Meeting, March 15, 1928

JOHN FAVILL, M.D., *President, in the Chair*

DIABETES MELLITUS IN DISORDERS OF THE HYPOPHYSIS. EUGENE F. TRAUT, Oak Park.

In the first four cases of acromegaly described, by Marie, two patients had sugar in the urine. Two years previously, Loeb had commented on the frequency of glycosuria in patients with tumor of the pituitary gland. Borchard found that glycosuria was noted in 50 per cent of the case reports of acromegaly.

The anterior lobe of the hypophysis is derived, like the pancreas, from an outpouching of the primitive gut. The effects of its endocrine secretion on sugar metabolism, even the existence of such a secretion, are not universally accepted.

Extract from the posterior lobe has been reported as lowering the blood sugar of rabbits. It will prevent and abolish the hypoglycemia of an injection of insulin. Extracts from the anterior lobe do not affect the blood sugar. Transient hyperglycemias have been produced by stimulating the hypophysis or the surrounding brain structures and by operations on the gland. It is impossible to separate the results of such manipulations from the inevitable trauma and irritation of the base of the brain. In this region lie tracts and nuclei having to do with heat regulation, water distribution and sugar metabolism. None of such proceedings have succeeded in producing a permanent dysfunction comparable to diabetes mellitus.

Krause's explanation of diabetes by pathognomonic changes in the pituitary loses its force in view of the frequency of small tumors and other pathologic changes in nondiabetic persons dying of any cause. Cushing's theory of the glycosuria in acromegaly is far-fetched but widely accepted. Acromegaly is constantly associated with eosinophilic adenomas of the anterior lobe of the hypophysis. Erdheim accepts Cushing's theory that increase in eosinophil cells in the anterior lobe represents hyperpituitarism.

REPORT OF CASE

CASE 1.—G. W., aged 79, had had the first acromegalic symptoms thirty years before. The chief complaint had been disability from stiff joints; they snapped on bending; they were never swollen or red. Sugar was found in the urine five years before presentation. Polyuria has been moderate. He is still sexually active, having intercourse nightly; there has never been any lull in his sex life. He has never had headache or vomiting.

He presents an appearance characteristic of an acromegalic patient. X-ray studies show an enlarged sella. The joints give roentgenologically the appearance of hypertrophic osteo-arthritis which is so common in acromegaly and due, not to inflammation, but to enlargement of the bone ends. The visual fields are narrowed, and optic atrophy has advanced perceptibly during the six months of hospitalization.

The diabetes is of the ordinary type. It required insulin for control; it did not show any unusual features to characterize it as hypophyseal.

Many investigators have remarked on the unexplainable sugar variations in diabetic acromegalic patients. In some of the cases followed over long periods, the diabetes has improved with the progress of the acromegaly.

CASE 2.—Miss M., a school principal, has a hypophyseal tumor which has apparently been arrested by x-ray treatment. She does not show any signs of acromegaly. Her diabetes has otherwise presented nothing to mark it from any other severe diabetes mellitus.

The pancreas in diabetes has long been the object of intense scrutiny by pathologists. Joslyn summarized the observations in his own cases as insignificant. Perhaps the pancreatic secretion is secondarily affected by organic changes far distant, as at the base of the brain or in adjacent structures.

DISCUSSION

DR. PETER BASSOE: In regard to the second patient, when I first saw her, in 1917, she had optic neuritis, and it was then reported that the sella was normal. Five years later, Dr. Hollis E. Potter reported that the sella was increased in size, that its floor appeared to encroach on the roof of the sphenoid, and that there was increased density of some of the structures inside the sella and adjacent to it. There has been little change during the last six years. I agree with Dr. Traut that there is a pituitary lesion, and I think that the large amount of radiotherapy of the sella had some good effect on the disease.

DR. TRAUT: I shall continue to follow this acromegalic patient, and I feel sure there is a possibility of discovering something. Every time one sees a case of this sort, it seems to me that one has an opportunity of uncovering the real pathology of diabetes.

SUBJECTIVE SENSORY DISTURBANCES IN PERIPHERAL NERVE LESIONS. LEWIS J. POLLOCK.

Severe and persistent formication, pins and needles and prickling and crawling sensations, are comparatively rare despite the accepted statement of their common occurrence. Pain, excluding causalgia, does not often result from injury of a nerve after the initial trauma. Concomitant vascular lesions were not found to be a source of pain in this series of cases. Subjective sensory disturbances were observed in a surprisingly small number of cases. Of 600 cases seen some months after injury only 161 were found to have sufficiently striking evidence to warrant an analysis of the history. Mild paresthesia may be present at some time in many cases, although the numbness complained of cannot be classified as such. The coexistence of diffuse injuries to other tissues in patients seen immediately after injury often masks a mild paresthesia. Frequently, the patient experiences some objective sensation at the moment of injury. It is likely that pressure of work at the base hospitals, as well as concomitant severe injuries to other tissues,

explains the absence from records of some 500 patients seen soon after injury of notations of any considerable number of cases showing subjective sensory disturbance. Pain was seldom complained of, except in a few cases of causalgia, and it was noted that causalgia and other subjective sensations appeared in partial lesions with the return of some motor power. A characteristic note in the history was as follows: "One month after injury, formication and tingling over the ulnar distribution developed and gradually increased, so that it was most severe two months after injury; since which time the sensation has diminished considerably." Or, "at the seventh week, formication appeared in the thumb and index finger, and at the same time motion began to improve." Paresthesia often occurred when pain was complained of, but hyperesthesia was usually associated with the burning pain occurring in causalgia. True tactile hyperesthesia was never present. An excessive reaction to painful stimuli evoked that peculiar sensation, known as "hyperpathic," constantly found in areas of overlap when sensation to pain had returned and tactile anesthesia was present. Pain, exclusive of causalgia, does not often result as a consequence of lesions of the peripheral nerve after the initial trauma. In most of the cases in which pain was noted, either the median or internal popliteal nerve had been injured, and in only two cases of complete section of the median nerve was there any pain. In general, as with paresthesia and hyperesthesia, pain was observed largely in incomplete or recoverable lesions. When several nerves were injured and the median or internal popliteal was included in the injury, the pain was distributed in the areas supplied by these nerves. The observations on cases of causalgia did not show any divergence from the experience of other observers. It may be said that many cases of causalgia are not associated with glossy skin, and that a considerable number of cases of glossy skin without burning pain occurred, making it probable that when the median or internal popliteal nerves are partially injured glossy skin or burning may occur, either alone or combined. The statistics regarding causalgia are unreliable, because in many instances severe burning pain has been designated as causalgia, whereas moderate or slight burning pain has not been so classified.

DISCUSSION

DR. FREDERICK HILLER: Will Dr. Pollock tell us whether there are not a number of observations showing that a causalgia may be treated successfully by section of the peripheral nerve combined with a periarterial sympathectomy? The suggestion of antidromic sympathetic nerve fibers in the anterior roots was already made by Lehmann in Giessen, who, however, did not find many followers.

DR. BASSOE: Does the study of the character of pain associated with arterial lesions of the extremities, with or without ischemic paralysis, throw any light on the pathogenesis of causalgia? This was brought home to me last week in the case of a man who had an injury to the knee in an automobile accident. When I saw him he had severe pain in the foot and glossy skin on the dorsum of the foot; no pulsation was present in the foot, in either the dorsal artery or the posterior tibial. The question came up as to whether the pain was due to a nerve injury or to a vascular injury. One frequently sees cases of threatened gangrene with severe pain and paresthesia.

DR. LEWIS J. POLLOCK: Soon after Leriche described periarterial sympathectomies for causalgia, a period of considerable enthusiasm ensued. During this period, speculation concerning the possibility of a direct pathway along the periarterial sympathetic nerves for the conduction of painful impulses occurred. It was found, however, that a continuous direct pathway did not exist. The disappearance of pain was frequently coincident with such vasomotor changes as vasodilatation with redness and heat in the extremity. When, as is usually the case, these vasomotor changes disappeared at the end of about three weeks, pain frequently returned. On the other hand, a number of cases have been observed following posterior root section in which the accompanying vasomotor disturbances persisted and pain stopped, and in some cases vasomotor disturbances disappeared

but pain persisted. All of this indicates that such experiments as have been conducted by Shaw on a possible antidromic fiber conducting painful impulses in the anterior root have some validity. Shaw was able to show that when a rabbit had been conditioned by experimental handling to show an awareness of stimuli to the ear, when the ear was rendered anesthetic by posterior root section the animal continued to signify his awareness when the ear was stimulated.

The frequency with which cases of gastric crises are unrelieved when the posterior roots are sectioned supports the thesis of the existence of an antidromic fiber for pain, and it is in these cases that, in contrast to superficial lancinating or shooting pains, deep boring pains are present. Whereas the superficial pains are easily localized, the deep boring pains are diffuse and unlocalizable.

What is true of the failure in causalgia is likewise the case in Raynaud's disease, Buerger's disease and other forms of dysesthesia.

MULTIPLE MELANOTIC TUMORS OF THE NERVOUS SYSTEM. S. E. BROWN and PETER BASSOE.

Clinical History.—A man, aged 37, was first seen by Dr. Bassoe in consultation with Dr. B. Beers at the Grant Hospital on Sept. 13, 1927. Two months previously he had begun to complain of pains in the legs and about the shoulders. Three weeks later headache developed. About the middle of August, he became unable to walk without help. For two weeks prior to admittance he had complained of diplopia, generally vertical, and of difficulty with micturition, first incontinence and for the last four days retention. He had vomited frequently for six weeks.

Examination.—The right pupil was sluggish to light; the left was normal. Vision in the right eye was poor, so that the patient could read only the headlines with this eye. Diplopia was present on looking to the left or downward. The right disk was blurred and much swollen, the left slightly blurred but scarcely swollen. Moderate stiffness was present in the neck. There was no gross cranial nerve palsy. The left leg was weak. Considerable ataxia was present in the arms and legs, more in the right leg. The superficial reflexes were normal; all tendon reflexes were absent. Sensation was normal.

Course.—The legs became weaker and more painful. Several attempts at lumbar puncture were unsuccessful, no fluid being obtained, though the needle appeared to enter the canal. Within a week the headache ceased. Paralysis in the legs was complete by the end of September. On September 30, Dr. Kraft found swelling of 2 diopeters in the right disk, and the fields of the right eye, especially the temporal one, were much contracted. After October 1, there was gradual loss of sensation in the lower extremities and buttocks, and bed sores began to develop. The right eye became blind, and the right pupil ceased to react to direct light, but reacted consensually. Vision in the left eye failed gradually during November. Pain in the legs, particularly in the left foot, remained troublesome even after sensibility was almost lost in both legs. The patient gradually failed and died Dec. 27, 1927.

Diagnosis.—No definite clinical diagnosis was made, but Dr. Bassoe suspected a condition related to the "multiple degenerative softening" described by Hassin and himself, or a combination of myelitis and optic neuritis, which has been described as "neuromyelitis optica" and which has generally been considered related to encephalitis or so-called acute multiple sclerosis.

Pathologic Report (Dr. S. E. Brown).—At a postmortem examination the body was pale and emaciated. A grayish red tumor was found in the lumbar cord and cauda equina reaching from the twelfth thoracic vertebra to the upper part of the sacrum. This tumor entirely filled the bony canal and infiltrated the nervous structures to such an extent as to destroy all anatomic relations. The dura here was replaced by tumor except in the upper one-fourth; above this, for a distance of 10 cm., numerous white tumors were found attached to the dura. The spinal cord was not pushed to one side but was located in the center of the tumor mass. No tumor nodules were found in the upper thoracic or cervical cord.

In the brain two grayish-white tumors were found on the inner side of the dura of the cerebellum, one on either side at the outer margin, measuring 1 and 1.5 cm., in diameter, respectively. The brain stalk of the hypophysis contained a similar tumor 8 mm. in diameter. A row of tumor nodules were found in the region of the exit of the fifth cranial nerve on the right. Only one white tumor nodule, 1 cm. in diameter, was found in the brain substance, located in the fissure of Sylvius at the junction of the cortex and medulla at the level of the third ventricle.

White metastatic nodules, from the size of a pinhead to that of a pea, were found in the lung, myocardium, endocardium and peritoneum. Many elevated cup-shaped tumors were found on the lining of the jejunum. The liver did not contain any tumor nodules. The eyes were not examined. The right lung was solid with pneumonic consolidation, and in the apex was a large abscess cavity. The urinary bladder was markedly hypertrophied.

Histologic Observations.—The tumor is made up of oval or polyhedral cells with large vesicular nuclei. In places where the cells are compressed they are spindle-shaped. In the tumor of the cauda, some of the nodules in the myocardium, lung, and intestine, many of the cells contain deep brown pigment granules. Many of the nodules in the dura, brain, brain stalk of the hypophysis and myocardium contain few if any pigmented cells. Mitotic figures are numerous in all the nodules. The arrangement of the cells varies greatly, from solid masses of cells, distinct alveoli in places, to solid cords. The cells have a tendency to accumulate about the blood vessels.

Comment.—From the pathologic observations the tumor appeared to originate from the eye, but when one considers that after several examinations of the eye by competent physicians a tumor was not found clinically in the eyes, and then considers what an enormous tumor was found in the cauda equina, the latter is more likely the primary tumor.

So the case may be considered a melanoblastoma of the cauda equina (origin probably in the leptomeninges of the lumbar cord) with metastases to the dura mater, brain, brain stalk of the hypophysis, lungs, myocardium, endocardium, peritoneum and jejunum.

DISCUSSION

DR. G. B. HASSIN: The preliminary examination of the spinal cord showed marked involvement of the cauda equina with many of its bundles destroyed. The meninges were also affected, including their spaces and the roots. In contrast to widespread meningeal involvement, the spinal cord was but little affected except for its lowermost portion. Dr. Brown's assumption that the tumor originated in the cauda equina is correct and also corresponds with the clinical symptoms outlined by Dr. Bassoe. The inability to get the spinal fluid may be explained by the complete obstruction of the subarachnoid space which was packed with tumor cells. There were many more interesting changes in the cord as well as in the surrounding tissues which much resembled tabes; study of them may help in understanding the pathogenesis of this disease.

DR. R. G. JAFFÉ: I suggest for the tumor demonstrated by Dr. Brown the term "melanoblastoma." Two types of melanotic tumors are usually distinguished, melanocarcinoma and melanosarcoma. There is, however, no sharp borderline between these two types as demonstrated by the present case which in some places shows the histologic features of a sarcoma while in other places those closely resembling a carcinoma. The saromatous appearance of the tumor cells apparently is due to their crowding together in places where they meet with a greater resistance of the structures in which they grow and where the proliferative properties are marked. As to the primary tumor, I fully agree with Dr. Brown in calling the case a melanotic tumor of the cauda equina.

DR. BROWN: I wish to emphasize that even with the numerous metastases in the jejunum there was no sign of metastasis in the liver, either grossly or microscopically.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, March 23, 1928

N. W. WINKELMAN, M.D., *President, in the Chair*

THE NATURE OF THE REFLEX AS SEEN IN DEVELOPMENT. Presented by DR. GEORGE E. COGHILL.

Dr. Weisenburg has asked me to discuss the anatomic side of the subject. I have been studying the problem for twenty-five years, but it is only within the last two or three years that I have been able to concentrate my entire time on it. The work is extremely tedious. I have had to make all my observations under high power, oil immersion lenses and with the best kind of illumination, much of the time using color screens.

At a time when *Amblystoma* begins to swim, there is little conductive substance in the brain and spinal cord, and it is only by careful study that one can make out the conduction paths. I studied for several years before I could find where the motor fibers come from. I had the conventional picture in my mind of a motor fiber arising from a nerve call and passing directly out of the cord, but I could not find such an arrangement. Finally, there stood out before me a longitudinal tract neuron with an axon going down the cord and a branch going out of it to the muscle. Such an origin of motor fibers had never been recognized before. That shows how difficult the anatomic problem has been.

Dr. Weisenburg mentioned the corpus striatum. There are no nerve cells in that part of the brain when the animal begins to swim. There is a connection from the cerebral hemisphere to the olfactory center, and another from the olfactory center to the preoptic region. There is a path also that goes back from the preoptic region to the hypothalamus. From the postoptic region fibers run into the region of the nucleus of the fasciculus longitudinalis medialis. The latter tract continues to the motor tract of the spinal cord. The median longitudinal bundle is virtually continuous with the spinal motor path. In later stages it has to do with the reflexes of the eyes. In earlier stages, it relates to the trunk movement, when the animal does not have any limbs, tongue or eye muscles. But it is not essential to swimming, for one can cut the animal in two at the level of the auditory vesicles and the trunk will swim alone.

Those conditions which bring out the individual reflexes develop in the central nervous system long before the results of their action appear in behavior. In the rat, for example, when it begins to move, or before, one will find forebrain bundles well developed, and highly developed centers in the midbrain.

I was interested in the remarks regarding the latest reflexes to develop being the first to be affected by pathologic processes. A similar principle is demonstrable in *Amblystoma,* as when an *Amblystoma* embryo that can swim is placed in a solution of curare. When so treated the reactions pass out in the reverse order to that according to which they appeared in development; and when the animal is replaced in water it rapidly recapitulates the original process of development.

DISCUSSION

DR. GRAYSON P. MCCOUCH: The chief source of difficulty in the analysis of reflexes is the baffling complexity of the structures involved. By the selection of a simple form and by a comparison of its development of structure and function from its embryonal beginning to its maturity, Dr. Coghill is overcoming this difficulty and throwing new light on what we have regarded as the least accessible phase of the problem.

Dr. Coghill has asked me to discuss the bearing of his work on the mechanism of the coil reflex and of the "S" reflex in *Amblystoma.*

During the coil stage, there are both exteroceptive and proprioceptive contralateral reflex arcs, but no ipsilateral arcs. These contralateral arcs consist of

three series of neurons, all of which are common to both exteroceptors and proprioceptors, which are supplied by branches of the same afferent neurons. It is probable therefore that exteroceptive and proprioceptive reflexes begin to function at about the same stage of development. In that case, the coil stage may be characterized by two contralateral reflexes: (1) a tonic postural proprioceptive reflex; (2) an exteroceptive coil reflex.

The slow onset and prolonged character of the coil reflex may be due not only to the early stage of development of the muscles and neurons, but also to the fact that the movement is mechanically opposed by the tonic contraction of the muscles on the side of the exteroceptive stimulus. The resulting increase in tension in the muscles of the convex side may set up proprioceptive stimuli which accentuate and prolong the coil reflex.

The development of the "S" reflex is associated with the growth of collaterals from the final effector axons which turn back to end about cells of the floor plate. The fact that similar collaterals exist in the mammal and that stimulation of the central end of a cut anterior root does not produce any contraction suggests that these recurrent collaterals are inhibitory in function. Their anatomic relations suggest that their reflex effects must be practically synchronous with those of the main branch of the axon from which they arise. At this stage, an exteroceptive stimulus gives an initial wave of flexion to the contralateral side, of rapid onset and brief duration. The rapid onset may be due in part to reciprocal inhibition of the muscles on the side of the exteroceptive stimulus, which removes opposition to the initial flexion. The initial flexion may then be limited to a transient wave by autogenous inhibition from a secondary proprioceptive reflex stimulated by the initial contraction. This proprioceptive reflex, arising in receptors of the contracting muscles on the concave side, not only may cut short their contraction by impulses returning along the recurrent inhibitory collaterals, but may also excite the muscles of the convex side where efferent neurons may be passing from a state of inhibition to one of postinhibitory exaltation (successive spinal induction). Thus, an exteroceptive reflex may be followed by a series of proprioceptive reflexes or swimming movements analogous to rhythmic stepping reflexes in the spinal mammal.

DR. ALBERT C. BUCKLEY: One of the problems of interest in neurology relates to the priority of the appearance of the nervous system. Modern physiology regards the nervous system as a "further structural and functional expression of protoplasmic behavior" (Child). Cellular activity is an expression of excitatory behavior (excitomotor) as in muscle and gland. Energies which excite the organism into activity are the resultants of the interaction of forces within the organism and forces of the environment. To provide and maintain for contact between the environment and the neuraxis the nervous system obviously must originate from the ectoderm. Furthermore, the priority of development of the neuraxis provides points of origin of nerve supply to the visceral systems later to be developed. Furthermore, for protection of the neuraxis of vertebrates (osseous and others) obviously the nervous system is laid down before its protective coverings.

Early in the embryo there are evidences of excitomotor activity. In fact, the earliest is seen in intracellular activity in the ovum during maturation and fertilization. The earliest differentiated excitomotor activity, as described by Stewart Paton and others, has been seen in muscles of the heart before the appearance of neurofibrils.

The paralyzing (inhibitory) effect of noxious substances, such as cocaine and chloretone, is absent in primitive protoplasmic activities in vertebrates (muscle of the heart) until nerve fibrils have grown into the muscle. This would seem to indicate that the primary function of that nerve supply is inhibitory.

Patterns of reflex behavior appear to be mapped out early in the embryo, as observed by Minkowski: for example, flexion and extension of the extremities

movements resembling respiratory acts, opening and closing of the mouth, the Babinski response, movements of the eyelids and elevation of the chin as in swallowing.

Inhibitory functions controlling and regulating the activity of reflexes is evidently of later development. Without inhibitory influences, cellular activity is continued. Inhibition may be brought out as the result of: (1) antagonistic arrangement of muscle groups (flexion-extension); (2) differences in intensity of stimuli, the stronger inhibiting the weaker; (3) internal stimuli, instinctive and emotional, determining the attitude of the organism toward the source of stimuli, (4) effect of ideas (education and experience) in higher organisms.

Certain reflex, instinctive and emotional responses are recognized as fundamental in human behavior. Such responses connote certain types of experience as sucking, grasping and shrinking. Emotional states arise with instinctive dispositions, e. g., anger, self-abasement and self-assertion.

Psychiatric Applications.—In advanced organic dementia, when voluntary movements may be absent yet no organic paralysis be present, the swallowing and sucking reflexes are preserved and may be elicited by stimulation of fifth, seventh and ninth cranial nerves. Occasionally, a visual stimulus is sufficient. The grasping reflex is strongly active, and may be evoked by touch stimuli, as in attempting to move or arrange the clothing of the organic dement, the patient's hand clutching whatever may be near. To inhibit this reflex some other reflex must be activated.

The dominance of primitive flexor response is striking in states of deterioration and mental depressions. In some instances flexion becomes so pronounced as to cause the patient to assume the fetal position. In states of exaltation with attitudes of superiority, disdain or anger, the dominance of extensor response appears. In schizophrenia, many reactions are distinctly reflex and automatic in type. Impulsive reactions to relatively unimportant stimuli, apparently without provocation, such as aggressiveness and destructive acts, would appear to be of the reflex type uncontrolled because of lack of inhibitory influence.

In general, it may be stated that the reflexes appearing earliest in the order of functional development are apt to be the last to disappear in the process of functional disintegration. In a similar manner the last to be acquired are likely to disappear early in the course of the dementia.

When inhibitory influences are removed as the result of functional disintegration, primitive reflexes control the types of response to such an extent as to make them stand out conspicuously (Brain **50**:573, 1927).

SOME CLINICAL OBSERVATIONS ON THE VALUE OF THE HOFFMANN SIGN. Presented by DR. TEMPLE FAY and DR. HENRY B. GOTTEN.

This study comprises observations made on 1,017 persons in whom the so-called "Hoffmann sign" or "digital reflex" was tested in conjunction with the Babinski sign. Of this group, 393 normal subjects were studied from the student body of the University of Pennsylvania, and in this group were found twenty-one positive responses to the Hoffmann reflex and fourteen positive Babinski signs. It is interesting to note, in this small number of apparently normal students showing positive Hoffmann or Babinski signs, that thirteen of the subjects gave a history of former trauma or injury, meningitis or epilepsy.

In another group of 285 persons studied on the medical wards, without definite organic disease of the nervous system, only two positive Hoffmann signs were obtained, so that in the normal and in those suffering from conditions other than involvement of the central nervous system, only an exceptional positive response was obtained.

In a group of 339 patients showing definite organic disease of the nervous system, 132 showed a positive Hoffmann reflex. In the 118 patients with hemiplegia studied, eighty-two showed a positive Hoffmann and seventy-six gave a positive Babinski sign. In fifty-one patients suffering from tabes and paresis,

eight showed a positive Hoffmann and sixteen a positive Babinski sign. In twenty-seven cases of arteriosclerosis, a positive Hoffmann was found in eight and a positive Babinski sign in five. A full chart and percentage will appear at the time of the publication of the paper.

The outcome of this study seemed to indicate that the Hoffmann sign was a delicate reflex phenomenon associated with organic disease of the nervous system, and that this reflex responded to lesions situated above the midcervical region or those that were focal to the cortical centers of the arm and hand. The Hoffmann reflex was obtained in some cases in which the Babinski sign was absent. Crossed phenomena were noted as well as bilateral manifestations in a small proportion of the cases studied.

Conclusion.—The Hoffmann or digital reflex is a valuable adjunct to the clinical study of organic diseases of the nervous system. Its reliability may be placed with that of the Babinski sign, and the routine use of this reflex should find wider clinical application.

DISCUSSION

DR. TEMPLE FAY: Regarding the series presented by Dr. Gotten, I think that a great deal of credit should go to him for his work in finding these cases, classifying them and checking each case with the diagnosis, and as far as possible, establishing a relationship between the Hoffmann and the Babinski sign. We were struck by the fact that the Hoffmann was more reliable than the Babinski sign, in an apparently normal person, when the Hoffmann sign was present to indicate intracranial pathologic changes. Thirteen patients had a history sufficiently suggestive to imply a definite cerebral lesion. We could not find a report by Hoffmann himself and do not know whether he discovered the reflex phenomenon, which is obtained by snapping the middle and ring finger-nail, or whether he was the only one to describe it.

A CASE OF MOTOR APHASIA WITH AUTOPSY. Presented by DR. ALFRED GORDON.

To recapitulate Marie's revision of aphasia versus the classic Broca's center for aphasia, the following statements may be recalled: Marie's lenticular zone covers a square area limited anteriorly by the white substance of the third frontal convolution, posteriorly by Wernicke's area, externally by the insula and internally by the wall of the third ventricle. It comprises, therefore, the external capsule, the lenticular and caudate nuclei, the anterior and posterior segments of the internal capsule and also the optic thalamus. According to Marie, the lenticulostriate ganglia, either by themselves or through their afferent and efferent pathways, represent in the mechanism of language a body far more important from a motor standpoint than the cortical center of the old view of Broca. He says that the lenticular nucleus plays an enormous rôle in phonation and in coordination of movements indispensable for articulated speech; that a lesion in any spot of the lenticular zone will produce symptoms of aphasia (sensory and motor). From a careful analysis of a large number of anatomoclinical cases, Marie came to the conclusion that the division of aphasia into motor and sensory is no more tenable than the theory that there is only one aphasia, namely, sensory aphasia to which anarthria is sometimes added. Since Marie's announcement, a large number of anatomoclinical observations on aphasia have been reported by competent observers, some corroborating and others denying the foregoing view.

The case here reported seems to oppose radically the new contention of Marie. The brain shows a large softened area confined strictly to the left third frontal convolution, infringing somewhat on the ascending frontal convolution but not posteriorly to the rolandic fissure, therefore leaving intact the "lenticular zone." During life, the patient presented a mild right hemiplegia and a typical motor aphasia. The case is as follows:

M. S., a middle aged woman, married, had been complaining for several months of a dull pain in the head and of dizziness. One morning, on awakening, she

was unable to make herself understood; her words were not clear and she substituted one for another. At the same time the right arm and leg were weak. There was no loss of consciousness. This condition remained unaltered for fifteen days. When she came under my observation the following condition was observed: The right hemiplegia was not pronounced. There was only a slight degree of rigidity, more in the arm than in the leg. The face was also slightly drawn to the left side. The tongue protruded toward the right. The pupils were unequal, the left being larger than the right. The patellar tendon reflexes were increased on both sides. There was no ankle clonus on either side, and the plantar reflex was occasionally extensor on the right side but most of the time indifferent by various tests; it was flexor on the left side. Sensations were normal in every respect all over the body. The lower abdominal reflex was extremely slight on the right side, but marked on the left. In walking she dragged slightly the right foot. The right arm was paretic, more than the leg on the same side. The right biceps and triceps reflexes were increased; they were normal in the left arm. Astereognosis was not present. Other deep sensibilities were not involved in the right upper limb. The sphincters were intact. The eyegrounds were normal, except for a marked angiosclerosis. Palsy of the ocular muscles was not present.

The most conspicuous manifestation was the speech disorder. There was no anarthria. The words were well articulated, and phonation was good. The words could be understood. This condition showed at once that the muscles of phonation, namely, those of the larynx, pharynx, lips and tongue were intact. The patient was unable to express her thoughts by speech. There was a considerable loss of spontaneous speech. She could pronounce one or two words at the time and frequently repeated the same words. Occasionally, she would use extremely short sentences, such as "All right," "Good morning," "Good-bye," "I am," "Not good." There was also noticed an inability to modulate the voice, which was invariably of the same tone. Reading and repeating words presented the same characteristics. She understood perfectly printed, written or spoken words or sentences. The mental image of articulation of words was intact; the inner language was preserved, as the patient in various ways demonstrated her knowledge of the number of syllables or letters in each word; one of them was that she showed them on the fingers of the left hand. Under dictation she was able to write correctly, which she did with the left hand, although not skilfully; she was right-handed. The absence of word deafness (as the patient understood when spoken to) and of word-blindness (as the patient could understand printed or written words and sentences) which is characteristic of sensory aphasia (Wernicke and Dejerine), classifies the speech disorder of this patient as "motor aphasia," and as "pure motor aphasia" in view of the integrity of the inner language. The further course of the disease in this case did not present special alteration from that described. The condition lasted seventeen months, when she accidentally fell, fractured her right leg, became comatose and never rallied. During the illness all laboratory tests were made with negative results, except a slight anemic condition, with hemoglobin 75 per cent and red cell count 3,700,000. Urinalysis, blood sugar and blood urea were all normal. The spinal fluid was not examined.

At autopsy, both kidneys were found contracted; the left ventricle was dilated, the aortic valves calcified and many blood vessels were sclerosed, especially those of the circle of Willis at the base of the brain. The most interesting observations were those in the brain. Before a section was made, the left third frontal convolution was found to be soft under the finger. An anteroposterior section revealed a large softened area under the cortex of the third left frontal convolution, involving to a slight extent posteriorly the subcortical tissue of the ascending frontal convolution. It is therefore evident that the cerebral symptoms observed during life find complete and mathematically exact justification in the pathologic changes of the brain. The case did not present symptoms of sensory aphasia, and the classic centers for the latter were found to be not involved. On the other hand, Marie's "lenticular zone of language" was intact.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

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WALTER M. KRAUS, M.D., *Chairman of the Section, in the Chair*

A CASE FOR DIAGNOSIS. DR. IRVING H. PARDEE.

Clinical History.—A man, aged 34, was admitted to the Neurological Institute on Jan. 24, 1928, complaining of complete blindness in the right eye since the age of 13, partial blindness in the left eye since the age of 15; tremor of the hands and arms, and difficulty in walking for two years. The course of the illness was intermittent and progressive as well as regressive. At the age of 13 the patient began to have failing vision in the right eye. He went to the New York Eye and Ear Infirmary intermittently for two years. At the end of that time vision in the right eye was entirely gone and that of the left eye began to be blurred. He was examined by Dr. Weeks who reported vision in the left eye as 20/60. He was sent to Dr. Coakley for examination of the nose and throat and after an x-ray was taken of the head, he was sent to the New York Eye and Ear Infirmary where he was given four injections of arsphenamine, which seemed to improve the condition of the left eye. This was four years after the onset of the illness. Just after this the patient began to have a coarse tremor in the right hand, which cleared up with rest in the country after it had lasted for from six to nine months. Two years later he was at Bellevue Neurological Clinic and was given twenty or more injections of mixed treatments. Four years before admission, he had had a gonorrheal infection which left him with a stricture. He says that when sounds were put in to break up the strictures, he became so nervous that he again developed tremor of the hands, first of the right and then of the left. The tremor of the left forearm was never marked until about four years prior to presentation at the institute. Now he cannot lift a cup of coffee. The tremor is of the intention type, that is, absent while at rest, improved after a night's rest and much worse when the patient attempts to use the hands.

During the past year he has noticed that he walks unsteadily in the street; people ask him why he staggers and walks so crookedly; he cannot run for a street car, and his knees get weak and trembly when he is excited. Since the summer he has been unable to walk down stairs without support. Pain has not been present in the arms or legs. He has involuntary twitching of both arms and legs at night; he can still control this to some extent. At times the speech is thick and the voice shaky, especially when he is excited. The family denies any change in personality. The patient is rather euphoric at times, especially when giving his history; he talks about himself. He is also emotional and several times burst into crying. He has been told that all his nervous symptoms are the result of masturbating.

About two months prior to presentation the blood was tested by the board of health, and the reaction was reported as 1 plus. His physician said that he had cerebrospinal syphilis and gave him four injections of bismuth. He has occasional headaches.

Physical Examination.—The patient is well nourished and well developed, appears about 20 years of age (actual age 34), and is cooperative though not very intelligent. The right eye is rotated upward and inward. He is rather restless and talkative, and there is a slight tremor of the head, body and extremities. The gait is slightly spastic. There is tremor of the arms and head in walking; the gait on the toes is normal, likewise on the heels; Fournier's tests are fairly done. The gait on a line is poorly done. Associated movements of the arms, trunk and head are obscured by tremors. The patient is right handed.

Standing with the feet together and eyes open or closed is normally performed; standing on either foot is normally performed. No Romberg sign is present. The

finger-to-nose test develops a marked intention tremor of the arms, more on the right than on the left side. The heel-to-knee and along shin test brings out intention tremor, more on the right side. The finger-to-finger test is fairly well done but causes intention tremor and spasticity, more marked on the right. There is no adiadokokinesis. The patient talks with a rather queer, jerky speech. There are coarse tremors on voluntary movement or exertion.

Reflexes: biceps, left 3+, right 3+; radial, left 3+, right 3+; triceps, left 3+, right 3+; ulnar, left 3+,, right 3+; wrist, left 3+, right 3+; patellar, left 3+, right 3+; achilles, left 3+, right 3+; upper lateral abdominal, left 0, right 2; lower lateral abdominal, left 1, right 1; cremasteric, left 1, right 1; Hoffman's sign, left +, right +; Babinski sign —; fanning, left ?, right +; Chaddock sign, left +, right 0; Oppenheim sign, left +, right +; Gordon sign, left 0, right 0.

The strength of the muscles is exhibited by the grip of the hands which is strong and equal. Marked hypertrophy of the biceps with some atrophy of the triceps gives a rather extraordinary outline to the upper arms.

Abnormal associated movements are not elicited.

No stiff neck or other abnormalities of meningeal irritation are noted.

A sensory examination does not reveal a definite level. There is slight diminution in vibratory sensation below the pelvis; slight tenderness is present over the sixth cervical spine.

Cranial nerves: The left pupil is slightly irregular and sluggish in reaction to light; the right pupil is also slightly irregular, and reaction to light is absent. Upward nystagmus is inconstant to the left; movements of the left eye are possible in all directions; the right eye does not move upward and is restricted in inward movement, and there is ptosis of the right lid. There is no facial asymmetry.

Mental Status: The patient is euphoric and loquacious; he is emotionally unstable and cries and laughs easily when spoken to.

Laboratory Studies.—Examination of the blood (Jan. 28, 1928) revealed: hemoglobin, 90 per cent; color index, 0.9; red cells, 4,700,000; white cells, 7,600; neutrophils, 67 per cent; lymphocytes, 32 per cent; transitional cells, 1 per cent; Wassermann reaction, negative; urea, 32.5 mg.; urea-nitrogen, 15.2 mg.; sugar, 0.085 per cent.

Examination of the spinal fluid revealed: cells, 3; globulin, 2+; protein, 125 mg.; colloidal gold, 000000000; Wassermann reaction, negative.

Urinalysis showed: a slight amber color; acid, 1020; albumin, 0; sugar, 0; indican, 0; a few leukocytes; a few epithelial cells; many bacteria.

X-ray examination of the skull showed that the pineal gland is calcified and occupies its normal position. The sella is fairly well outlined. Possibly the bridging noted has produced some constriction, so that the capacity of the sella has been reduced sufficiently to give rise to some pressure. The change does not resemble that of any pathologic lesion.

Examination of the spine shows the vertebrae clearly outlined and apparently normal.

Eye Studies.—Examination of the eye by Dr. Holden on Jan. 25, 1928, showed: vision, bare perception of light in the right eye; left 2/20; fields, left field complete; fundi, right shows complete atrophy of the optic nerve; some veins are tortuous, and there is a little disturbance of pigment about the disk; the right is normal. Pupils: right, 5 mm.; left, 3.5 mm. in diameter; right round in shape, left irregular; light reaction absent in the right eye but fair in the left; convergence absent in the right, present in the left; there is paralysis of each internal rectus; divergence is variable; there is moderate ptosis on the right and inability to turn the eye upward.

Conclusion.—It is difficult to say whether this is a simple or postneuritic atrophy.

Examination of the eyes on Jan. 30, 1928, revealed: vision, right eye—no light perception, left 20/20; fields, left normal for color and form; right, no field existing; fundi: right, complete white atrophy, simple; left, normal, slight pallor of outer portion, hardly to be considered pathologic. Pupils: right, 5.5 mm.,

slightly irregular, no reaction to light or convergence; left, 5 mm., irregular oval, partial reaction to light, poor to convergence, long axis at 135 degrees; nystagmus: right, none; left, none.

The interpretation of the case is that it is evidently a case of ophthalmoplegia externa. There is partial ptosis and partial paralysis of the superior and internal rectus in the right eye. Paralysis in the left eye is not present; there is no limited movement of the internal rectus.

DISCUSSION

DR. BERNARD SACHS: It is dangerous to discuss a case of this sort without having an opportunity of examining the patient. I think the differential diagnosis that Dr. Pardee tries to establish between disseminated sclerosis and cerebrospinal syphilis is perfectly justifiable. I think I would rule out syphilis, even if the patient does have a 1 plus Wassermann reaction. The spinal fluid did not show anything. Besides, a syphilitic process that had lasted this number of years without either showing greater variations or becoming much more progressive, would, I think, be extremely rare. Of course, it would be hard to disprove it. Comparing it with what I have seen and known of cerebrospinal syphilis, I am not inclined to jump at that diagnosis unless everything else is excluded.

I would not be willing to make a diagnosis of disseminated sclerosis and to let it go at that. The case does seem to me to belong rather to the category of widespread degenerative diseases such as occur in various form of family degenerative disease. The disease began fairly early in life and has been going on with comparatively slight changes. The fact that impresses me more than anything else, and it seems to me to take it out of the category of ordinary disseminated sclerosis, is the character of the intention tremor. It is really, to my mind, more a violent ataxic tremor and is a little different from the intention tremors of ordinary disseminated sclerosis. The possibility that this may be some form of family degenerative disease, of which there are a number of different types may be considered, particularly in view of a marked or complete optic atrophy in one eye. Those changes of the optic nerve also occur in various groups of symptoms in connection with all sorts of family disturbances, so that I think I should be rather inclined to put this case into the category of a somewhat indefinite degenerative disease of the central nervous system; possibly, one of the various types that have been described in connection with family diseases.

DR. PARDEE: As the patient went out of the room he said, "Is that Dr. Sachs?" I said, "Yes." He said, "Dr. Sachs saw me fifteen years ago." I wonder if that would alter your point of view? The early optic atrophy seems to be an outstanding feature of the disease. It was the one factor which led me to think it might be syphilitic; otherwise there is no proof of a syphilitic involvement except for the sluggish pupil on the left side. I welcome Dr. Sachs' suggestion as to the possibility of its being a familial disease. Although there is no familial history, there always has to be the first one in a family, and he may be that one.

A CASE REPORT OF TORULA MENINGITIS. DR. S. BERNARD WORTIS and DR. HENRY B. WIGHTMAN.

A. H., a man, aged 20, single, an American, a chauffeur by occupation, was admitted to Bellevue Hospital on Aug. 26, 1927, complaining of pain in the eyes and headache of three months' duration. His past history was essentially without significance. The father died of tuberculosis at the age of 27; the mother, two sisters and one brother are living and well. Three and one half months before admission to the hospital the patient noticed slight haziness of vision and headaches. The onset was insidious, and the headaches were not severe, nor were they present at all times. They became of increasing intensity and were associated with definite drowsiness and mental confusion. Three weeks before admission the patient vomited at the time when the headaches were most severe. The patient consulted an oculist who prescribed glasses, which gave no relief. He

was treated in the outpatient department for a "head cold," and was finally admitted to the nose and throat service with the diagnosis of sinusitis.

Physical Examination.—The man was fairly well developed and well nourished, and lay quietly in bed, apparently in pain but not acutely ill.

There was tenderness over the frontal sinuses on percussion; the pupils were normal; the fundi showed marked papilledema with exudation, hemorrhages and obliteration of both disks and distention of the veins; the nose resembled bilateral hypertrophy of the turbinates. Examination of the sinuses showed: the antrums were clear; the left sphenoid contained pus. The pharynx, larynx and ears were normal. The mouth and teeth were in a poor condition.

There was rigidity of the neck and it was painful on flexion.

The lungs and heart were normal.

The abdomen was normal.

There was weakness of the right hand and fine tremor of the left fingers with the arm extended. The left knee jerk was not obtained, the right was questionable.

The temperature was 99.8 F.; pulse rate, 84; respiration rate, 20. Blood pressure was 130 systolic and 70 diastolic.

The laboratory tests showed that the urine was normal. The blood count showed: red cells, 4,200,000; hemoglobin content, 80 per cent; white cells, 12,400; polymorphonuclears, 81 per cent; lymphocytes, 19 per cent. The chemical examination of the blood showed: nonprotein nitrogen, 30; sugar, 90; creatinine, 1.5. The Wassermann test was negative.

The spinal fluid showed: increased pressure; slight turbidity; cells, 180; 88 per cent, lymphocytes; globulin, increased; cultures revealed no growth.

A diagnosis of abscess of the left frontal sinus was made, and the patient was removed to the neurologic service.

An additional examination of the cranial nerves showed: first, no cooperation; second, fundi as already recorded, the fields showed concentric constriction; third, fourth and sixth, pupils normal, no nystagmus; fifth, eighth, ninth, tenth, eleventh and twelfth, normal; seventh, some peripheral weakness of the right side of the face.

Power and coordination were good in all extremities. There was no asynergia of the arms or legs. The station and gait were not tested. There was fine tremor of the left fingers with the arm extended.

Of the superficial reflexes: the corneals were present and equal; abdominal, weak and transient; plantars, normal; there was no Babinski sign; of the deep reflexes, the arm reflexes were present and equal; the knee, ankle and hamstring reflexes were greater on the right.

There were no changes in sensation.

There was no cooperation in position sense

The tache cérébrale was present.

The patient had a stiff neck and a bilateral Kernig sign.

Meningococcus meningitis was suspected because of the increasing meningeal signs. A spinal tap on September 5, ten days after admission to the hospital, revealed: a fluid with a glazed appearance; slightly increased pressure; globulin, 3 plus; sugar, absent; cells 540 per cubic millimeter, 90 per cent lymphocytes. A pellicle formed on standing. A stained smear did not reveal any organisms, and culture did not show growth.

Course.—The patient became increasingly drowsy. Antimeningococcus serum, 20 cc., was given intraspinally on September 7. The spinal fluid removed (40 cc.) showed a moderately cloudy fluid under slightly increased pressure; globulin, 3 plus; sugar, absent; cells, 600; 94 per cent, lymphocytes.

The Wassermann reaction of the spinal fluid was negative, the colloidal gold curve was 5554331000. A distinct pellicle formed on standing. A smear of this pellicle showed an occasional dark-staining, round body, the size of a small lymphocyte. The cells appeared also to be degenerated. Culture of the fluid showed multiple white elevated colonies appearing after forty-eight hours. Smear of these colonies showed round gram-positive bodies, which, after further incubation, disclosed the budding forms of yeasts. Mycelia were not noted. There was

no acid or gas noted in any of the following sugars: lactose, dextrose, maltose, saccharose, mannite or inulin. There was no acid reaction or coagulation in litmus milk. Repeated stainings by the Ziehl-Nielson method for the tubercle bacillus were negative.

Two cubic centimeters of the spinal fluid were injected into the peritoneal cavity of a guinea-pig at this time. The guinea-pig was alive and healthy after six months when it was killed. Observation of the guinea-pig at autopsy did not show any gross pathologic change. There was the suggestion of an inflammatory reaction about the site of inoculation; but on microscopic section this was found to be nothing more than a beginning degeneration of the recti muscles.

The antimeningococcus serum did not have any affect.

On September 8, 0.2 cc. of old tuberculin was injected intradermally and gave a local but no focal reaction. There was a slight rise in temperature to 100.2 F.

Throughout his stay in the hospital the patient's temperature remained at 100 F. with only two rises, one to 101.2 F. and the other to 102 F. The pulse rate remained at 80 and the respirations at 21.

Spinal taps were performed daily for the relief of pressure. The results were: On September 9, 20 cc. of cloudy fluid was withdrawn under increased pressure; globulin was 4 plus, sugar was absent, cells numbered 480 with lymphocytes 60 per cent. A pellicle formed on standing. Smear and culture were as previously noted. Specimens of this fluid were given to Dr. Josephine B. Neal, of the board of health laboratories in New York, who identified the organism as the torula by smear and culture.

The patient became noisy, restless, irrational and incontinent of urine and feces. He complained continuously of headache and stiff neck. Daily spinal taps from September 11 to the day of his death showed a cloudy fluid under increased pressure, globulin 4 plus, no sugar and 460 cells of which 60 per cent were of the lymphocyte type. On September 15, the day before death, the cell count rose to 1,600 with the same proportional differential count.

The patient was irrational, stuporous, lying with back arched and the neck stiff. He also had difficulty in swallowing fluids. He developed the signs of bronchopneumonia and died on the following day. Necropsy was refused.

Comment.—This is the twenty-third case of torula infection reported in man; nineteen of them have occurred in the central nervous system with fatal termination. The essential features of these cases are their insidious onset, their chronicity, the low grade of fever, the slow rate of the pulse and respiration, the negative blood and serologic observations and the changes in the spinal fluid. The latter closely simulate tuberculous meningitis with increased globulin, the absence of sugar, the relatively low cell count, the lymphocytosis and the pellicle formation. Accurate distinction is made only by the isolation of the torula organism either from the pellicle or from cultures.

Clinically, the picture is one of subacute or chronic meningitis or of an intracerebral lesion (tumor or abscess). There are no features characteristic of this type of infection. Diagnosis is possible only by detection of the organism in the spinal fluid or in the tissues at necropsy.

Dr. Wortis (in closing): I believe that some of the lymphocyte counts on the spinal fluid reported in the literature are relatively high because the torula organism is of the same size as the lymphocyte; in an unstained specimen it is easy to mistake one for the other.

The Syndrome of Diabetes Insipidus, Exophthalmos and Disease of the Membranous Bones. Dr. Louis Hausman and Dr. Walter Bromberg.

This unique symptom-complex is of particular interest in its bearing on the mechanism of diabetes insipidus and the possible relation of the latter to disease of the membranous bones.

The patient, a boy, aged 3½ years, had a history of exophthalmos, polydipsia and polyuria. The ancestry of the child did not reveal pertinent facts. At birth

the patient suffered apparently from asphyxia neonatorum and convulsions, following protracted labor. This condition disappeared soon after birth. Up to the age of 1½ years he had repeated attacks of bronchitis. At the conclusion of the last attack, measles developed.

The present illness began about one and one-half years prior to presentation when the patient was 2 years of age, at which time the mother noticed that the child was drinking and passing large amounts of water and that his eyes were becoming prominent.

Physical Examination.—On admission the boy measured 78 cm. but was well proportioned. The mental status was normal. There were: an astounding and progressive exophthalmos; bilateral Babinski sign; marked diabetes insipidus with an intake of about 6,000 cc. daily and a corresponding output. A roentgenogram of the osseous system revealed a remarkable picture in the skull, consisting of large sharply defined defects particularly in the frontal and temporal regions, as if the bone had been eaten away by a rongeur. The sella turcica was normal. The rest of the skeletal system was entirely normal. Sugar tolerance was definitely increased. The changes in the blood and spinal fluid were negative.

The condition took three courses: (1) progressive exophthalmos; (2) progressive dysostosis spreading to the parietal, orbital, malar and mandibular areas; sella, normal in all plates; (3) diabetes insipidus in which prompt relief was obtained with daily injections of pituitary extract. Various methods of treatments were tried. The only one of value was the pituitary extract, which influenced water metabolism. Ultraviolet radiation, calcium lactate, cod liver oil and parathormone were all tried without apparent benefit.

Comment.—A survey of the literature reveals twelve other cases. In each instance the membranous bones of the skull were involved, although in several cases other parts of the skeleton were also invaded. The disease occurs chiefly in children. The pathogenesis is unknown, although the incidence of antecedent infection is high. The course is progressive in most instances.

The evidence points to the tuber cinereum as the seat of the lesion, in which the tubero-infundibular mechanism is especially involved. The latter is apparently mediated through a bundle of nerve fibers from the nucleus supra-opticus of the tuber cinereum to the infundibular process, so that the latter is under the influence of the former. This functional and anatomic continuity is in keeping with the embryologic facts. The relation of this mechanism to the anterior pituitary lobe and to the process of growth, dysostosis, carbohydrate metabolism and adiposogenital dystrophy was also considered in the light of recent experimental data.

The conclusion was reached that the dysostosis may be interpreted as a parainfundibular manifestation. The study was extended to the consideration of some of the other osseous dystrophies: such as, the hereditary cleidocranial dysostosis described by Marie and Sainton, the familial craniofacial dysostosis described by Crouzon, and Paget's disease. A critical analysis of these conditions strongly suggests the possibility that they are all closely allied to the type described.

DISCUSSION

DR. SACHS: I believe that the majority of us will neither agree nor disagree. At least, the subject is entirely new. Dr. Hausman has done excellent justice to it and has done as much with it as one could possibly expect to do at the present time. One may agree to consider this as an entirely unique group of symptoms. Personally, I had never seen anything of the sort until I had the privilege, through Dr. Hausman, of seeing this child in the wards of the hospital. It is a combination evidently of a double and symmetrical exophthalmos, of diabetes insipidus, dwarfism and of a remarkable dysostosis.

I think it would be important, in order to fasten this one picture in mind, to try soon to give the syndrome a name that will at least refer to two or three of the prominent symptoms, either the diabetes, the exophthalmos, the dwarfism or the dysostosis. The dysostosis seems to me the most striking of all the condi-

tions in this case. That remarkable wearing away of the bone which perhaps, if it were not so extensive, would suggest what one occasionally sees, in small patches, even in syphilitic conditions. But this constant wearing away of the bone is unusual.

Next to the purely clinical interest of these unusual cases the interesting thing would be the interpretation of the symptoms. The one point that interested me was the attempt to explain the exophthalmos. I can hardly realize or visualize a condition in which exophthalmos is to be ascribed to the weight of the brain above pressing downward, the orbital plates having been worn off. The question is whether it would not be just as simple to ascribe it to blocking of the venous blood supply. The exophthalmos might be explained in much the same way, as the exophthalmos which follows some forms of sinus thrombosis; but this is more apt to be unilateral than bilateral. I am not disputing the possibility; but it would be unusual, indeed, to think of the brain practically invading the orbital fossae. One hypothesis may be as good as another. I think for the present one must think of the entire group of symptoms as an exhibition of dyspituitarism. Whether it is altogether due to the pituitary or whether the tuber cinereum has a rôle in it, I think that dysfunction of the pituitary is the significant factor. Whether the previous infection has any bearing at all on a case of this sort is a point that is difficult to judge.

DR. KRAUS: I have been extremely interested in reading an abstract of Dr. Hausman's paper and also in hearing his presentation, because it appears to me to be another step forward in making somewhat clearer a point which he has emphasized, the control of the glands of internal secretion by the central nervous system. Possibly the best way for me to discuss this case is to express an opinion by means of a lantern slide.

This simple diagram expresses a view in regard to the control of the entire body by the visceral nervous system and the somatic nervous system. It is known that there is a control by the somatic nervous system of somatic muscle, the ordinary activity of voluntary muscle. I presume, and there is much evidence on which to base the presumption, that the visceral nervous system has trophic control of the somatic muscle. And I am of the opinion that muscular dystrophy is frequently, at least, an evidence of disorder of this control. If one leaves the somatic effectors on one side, and passes to the visceral nervous system, which is represented as divided into glands and visceral muscle, one finds a double control by the visceral nervous system. One is kinetic; that is, it puts the structures into activity. The other is trophic; that is, it maintains their integrity. Now, with this idea in mind, this double control, kinetic and trophic, of both the visceral and the somatic structures, I shall return to Dr. Hausman's presentation.

Roussy, who has been quoted by Dr. Hausman, has recently been of the opinion that the region of the tuber cinereum is in control of the entire body with the exception of the bony system. Roussy specifically states that the bony system is controlled by the anterior lobe of the pituitary, and he does not believe that it is controlled in a trophic manner by the nervous system. I think there is a great deal of evidence to show that Roussy's opinion is premature.

In a recent paper, Perkins and I have taken issue on that point. Dr. Hausman's paper certainly confirms our views to a great extent. It would be highly illogical to believe that one system of the body, the bony system, is immune, as it were, to control by the nervous system, particularly when the skin, a closely related structure, is so definitely controlled by the nervous system. Thus Dr. Hausman's presentation brings up a point of considerable importance, envisaging the entire control of the body by the central nervous system in that it brings up the question of the trophic control of bones.

It seems definite from Dr. Hausman's descriptions that the combination of diabetes insipidus, encephalitis and bony disorders is indicative of lesions at least close to each other, which disorder the trophic control of bones, on the one hand, and the control of metabolic activity, such as the water metabolism, on the other.

The question of whether it is the pituitary gland or the tuber cinereum has been excellently emphasized by Dr. Hausman's quotation and demonstration of the work of Greving. It is known that there is a nervous pathway between the tuber and the pituitary; they are closely allied. Dr. Hausman has emphasized their anatomy. It is perfectly logical to assume that the visceral nervous system controls the pituitary gland, however close it may be to the tuber, as well as that it controls the liver or the thyroid or any other more distant endocrine gland. The mere fact that it happens to lie closely should not make it so difficult to conclude that there is a control of it by the nervous system.

The relation of dwarfism and diabetes insipidus interests me very much; some twelve or thirteen years ago I described a case of nanism of the Paltauf variety, with autopsy observations, in which there was a curious condition which at that time was not understood. I am frank to say, I do not understand it yet. The patient was a dwarf, a circus clown, in Barnum's Circus. He was admitted to Bellevue Hospital. He was a curious looking little fellow with a shrunken face, and looked much older than he really was; he proceeded to go into a state of coma and then ceased entirely to secrete water. We had the patient in a special room at Bellevue with special nurses. We were careful in controlling everything possible in the sense of water excretion, but there was no question that this patient had what I called at that time adiabetes. That is to say, there was no flow through, instead of a "flow through" which is what diabetes means.

At that time I looked up the literature of the Paltauf dwarf group and dwarfism in general, and I was surprised to find that the original description included a report of just such conditions as I found in this case.

I was also interested to find at autopsy that the pituitary gland was entirely degenerated. At that time little was known in general about the tuber, and I certainly knew nothing about it as an intern. Unfortunately, the nervous system was not examined. Nothing was done except an examination of the pituitary. The curious combination of dwarfism with this condition opposite to that of diabetes has some significance.

The problem of acromegaly and gigantism comes definitely into the problem as Dr. Hausman has presented it to you, because there is definite bony change which is grossly opposite to that of the dwarf's.

In closing the discussion of Dr. Hausman's presentation, I wish to express the opinion that it adds another stone to the mosaic being gradually put together, which is enlightening in regard to the relation of the visceral nervous system to the rest of the body. It emphasizes that the central nervous system in its visceral portion at the base of the third ventricle has a trophic control over the entire body.

Dr. John McDowell McKinney: The idea occurred to me that a possible explanation of this syndrome is to assume that the membranous disease of the bones is primary, giving a displacement of the brain substance sufficient to cause exophthalmos, which may conceivably produce traction on the infundibulum and hence produce the pituitary symptoms in the patient. This is a possibility which I would like to hear Dr. Hausman discuss.

Dr. Orman C. Perkins: I was interested in a case of a patient with dystrophy who was admitted to the Long Island College Hospital only yesterday. This case is that of a man, aged 17, presenting a typical Landouzy-Dejerine picture. The dystrophy was first noticed four years previous to the time of admission, and is accompanied by a typical Fröhlich's syndrome. One interesting feature about this young man is that he was a "blue baby" at birth; other than this his past history has been without significance. From birth he has had a unilateral exophthalmos and proptosis on the same side.

X-rays of the bones have not been taken. I hardly expect to find bony defects in this case and have not yet had an opportunity for laboratory work.

Dr. G. H. Hyslop: It seems reasonable to me to lay the cause of the exophthalmos to the same factors that produce the other vegetative disturbances in the

patient. The exophthalmos may well have an origin similar to the exophthalmos found in thyroid disease. The cause of that is still moot. I do not believe that in this patient it is due to local pressure.

DR. HAUSMAN: The question of giving the disease a name had not occurred to me. As the para-infundibular region appears to be the mechanism particularly involved, and since the dysostosis constitutes the most outstanding and characteristic feature of the syndrome, the designation "para-infundibular dysostosis" might be considered. In the present stage of knowledge, however, it would be wiser to avoid giving the condition any pathologic designation until the actual mechanism and pathogenesis are firmly established. Meanwhile, a purely clinical terminology is needed, one that will reflect the essential clinical features. I should like to propose the term—diabetic exophthalmic dysostosis.

As to the nature of the exophthalmos, I appreciate Dr. Sach's suggestion that it may be due to venous pressure from behind, although there is no other evidence of retro-orbital venous stasis. In this connection I should like to consider Dr. Hyslop's suggestion that the exophthalmos may be an expression of disease of the thyroid. Unfortunately, we were unable to study the basal metabolism because the child was too restless. There have been a few cases in which a basal metabolism test has been made, but there was nothing to indicate that the thyroid was involved. There are no clinical manifestations of hyperthyroidism in our patient.

To my mind, it seems that the pituitary body in a way bears the same relation to the nervous system, especially to the hypothalamus, that the thyroid bears to the autonomic nervous system.

It has been pointed out that in autonomic imbalance involvement of the thyroid is the culmination of the disease, that is, the end-result. It may be that the pituitary bears a similar relation to the tuber cinereum.

I am fully acquainted with the work of Dr. Kraus. I was much impressed with his account, in 1917, of two interesting cases of nanism. I remember distinctly that the patients in these cases showed not only disturbances in water metabolism but also an increased carbohydrate intolerance. I think that they are closely allied to the group considered this evening.

As to Roussy's theory ascribing the regulation of osseous growth entirely to the anterior lobe, I can merely state that Smith's work indicates that the tuber cinereum may at times be concerned with the rate of growth; he has demonstrated that in certain cases in which a lesion of the tuber cinereum has been produced in rats, the total length of these animals may be reduced; in other cases it may not be affected at all.

The question whether defect of the membranous bone may not be the first sign of the disease is hard to answer accurately. I cannot conceive of the bone pressure producing diabetes insipidus by picking out the tuber cinereum alone; that would require an exquisite localization of pressure or traction to bring out a defect in that particular part of the nervous system.

With regard to the case of muscular dystrophy, the presence of exophthalmos is interesting, for one knows that many of these cases are associated with disturbances of the endocrine glands. In fact, one group of observers has postulated that muscular dystrophy is a disturbance of the endocrine glands. That, however, is open to question. To what extent the endocrine factor is an element in the osseous dystrophies must remain for further investigations to determine; suffice it to say that in some forms it is a most important factor in the disease process.

TRAUMATIC PNEUMOCEPHALUS, OPERATION AND RECOVERY. DR. THEOPHILUS P. ALLEN.

In May, 1926, Dandy (*Arch. Surg.* **12**:949 [May] 1926) reviewed the literature on pneumocephalus and analyzed twenty-eight case reports, three of which were his own. In December, 1926, Bullock (*Surg. Gynec. Obst.* **43**:750 [Dec.] 1926) made a similar study, analyzing sixteen cases including one of his own and not

including Dandy's three. Since then Davidson (*Am. J. Roentgenol.* **17**:447 [April] 1927), Eggers (*Arch. f. klin. Chir.* **144**:121, 1927), Jeans and Villechaise (*Bull. et mém. Soc. nat. de chir.* **53**:1158, 1927), Jansson (*Acta radiol.* **7**:1, 1926), Richards (*Arch. Otolaryngol.* **6**:74 [July] 1927), Nessa (*Radiology* **9**:74 [July] 1927) and Levison (*J. A. M. A.* **88**:921 [March 19] 1927), have added eight cases. These, with the present report, make a total of thirty-eight cases. Of this group, fracture of the skull involving a frontal sinus was responsible for the pneumocephalus in twenty-three, or 60 per cent of the cases. The other causes were erosion of the walls of the ethmoid sinuses by chronic infection, erosion of the floor of the skull by a tumor, fracture through the ethmoid sinuses, fracture through the sphenoid sinus, fracture through the mastoid, operation on the mastoid and abscess of the brain caused by gas-forming bacilli.

The case reported is one of the twenty-three in which fracture through a frontal sinus was responsible for the pneumocephalus. All of these cases showed a striking similarity in the clinical picture and in the pathologic processes. The common symptoms were rhinorrhea, headache, mental confusion, dizziness, peculiar noises in the head, convulsions and hemiplegia. Papilledema occurred but was not particularly common. The x-ray generally showed a pocket of air in the substance of the frontal lobe, air in the ventricles and occasionally air in the subarachnoid space as well. Dandy considered that the sequence of events in the production of the pneumocephalus was as follows: The meninges and the cortex are ruptured at the time of the fracture and the injured cortex, pia and arachnoid become adherent to the dura. Then with periods of increased pressure within the sinus such as might be caused by sneezing, coughing, straining or even swallowing, air is forced into the substance of the brain and trapped by a valvelike communication between the dura and the fractured bone or a collapsable sinus tract in the soft tissue of the brain. With repeated periods of increased pressure, the air pocket enlarges and finally ruptures into the ventricle; there may be an additional communication with the subarachnoid space through which the air has access to the ventricles, or either of these conditions may exist alone. Our case is typical of its group.

Case Report.—A man, aged 42, who was admitted to the New York Neurological Institute on Sept. 18, 1926, had been found unconscious after his car had crashed into a post, two months previously. He was taken to a hospital where he was found to have an extensive comminuted fracture of the frontal bone. He was unconscious for three days, disoriented and confused for about four weeks, then he improved and was discharged on September 1. At home his family considered that he was normal except that he was inclined to talk too much. On September 8, ten days before admission and fifty days after the injury, while walking from his bed to the toilet a large amount of clear watery fluid suddenly escaped from his nose, and he became faint and suffered a severe headache. The rhinorrhea occurred repeatedly at irregular intervals, the headache persisted and the patient became progressively confused, disoriented and demented. He became incontinent of feces and urine, and had to be fed by spoon. Most of the time he lay quietly in bed as if in a mild stupor, but he was easily aroused and complained bitterly of headache. At times his mind seemed to be clearer, and occasionally he got out of bed and wandered aimlessly about the house.

Examination on admission showed that he was sluggish, untidy and had the peculiar expression of a patient with marked mental disturbance. He also exhibited a shallow defensive facetiousness. For example, when asked to show his teeth, he did not comply but remarked, "My teeth are not as good as yours." He could be persuaded to carry out only the simplest orders after much urging and demonstration. He exhibited no initiative, asked no pertinent questions and volunteered no information. Left to himself he lay quietly and was completely indifferent to his surroundings. Attention, concentration and judgment were markedly impaired; he was disoriented for time and place and showed no insight into his mental state. He walked with the feet widely apart in a slow uncertain shuffle. Over the right frontal region of the head the scalp and bone were elevated about 1 cm. to form

a triangular plateau, one edge of which was 5 cm. long, the other 6 cm. Percussion over this elevation gave a remarkably resonant hollow note. In the left frontoparietal region there was a shallow stellate depression over which the percussion note was more resonant than normal. On the right side of the body the deep reflexes were slightly increased, the superficial reflexes diminished. The Babinski toe sign was present, and muscle coordination and strength were slightly impaired. It was considered that these signs were due to the stellate depressed fracture over the left side rather than to a pneumatocele on the same side. The only neurologic disturbances on the left were paralysis of the lower facial musculature and a slight widening of the palpebral fissure. The patient could not recognize common odors. The optic disk margins were hazy, and the veins were engorged. The rest of the examination gave negative results.

Roentgenograms showed extensive stellate fractures of the frontal bone with one fissure through the right frontal sinus extending forward into the cribriform plate. The coronal suture was involved, and the right half of the frontal bone was separated at the bregma and slightly raised. There was a large pneumatocele in the right frontal lobe and air in the ventricular system. A shallow depressed stellate fracture was present over the frontoparietal region.

The spinal fluid was a dirty yellow; it contained 81 cells per cubic millimeter and 150 mg. of protein per hundred cubic centimeters of fluid. The other laboratory data were without significance.

On September 27, seventy days after the accident, the patient was operated on by Dr. Elsberg. Utilizing the old fracture lines and the elevated fragment of bone, a right frontal bone flap with its base placed anteriorly was turned down. The dura was found to be tense and covered by a layer of organized blood clot about 2 mm. thick. The right frontal lobe was then punctured and considerable air escaped; this reduced the tension of the dura. Next, the cortex was exposed by wide incision of the dura and found to be soft and fluctuating. The needle was again inserted, allowing more fluid and air to escape. The bulging right frontal pole was carefully separated from the dura; toward the mesial side there were some fine adhesions, and after these had been divided, considerable clear yellow fluid ran out. The surface of the frontal lobe now became concave so that little retraction was needed to bring the orbital plate into plain view. Other adhesions were separated, and just behind the frontal sinus a small perforation of the dura was found; it was about 2 mm. in diameter and was rimmed with a brownish discoloration about 1 mm. in width. A probe passed through this hole came on irregular bone, undoubtedly the fracture line in the posterior wall of the sinus. A piece of temporal muscle was placed over the perforation and a second piece over the opening toward the mesial surface through which clear yellow fluid had flowed. The cavity left between the dura and the brain by the collapse of the brain was filled with a solution of physiologic sodium chloride, and the dura was closed by a continuous silk suture. Along the edges of the old fracture line the bone was trimmed so that the edges approximated, and thus the old deforming elevation was removed. The incision on the scalp was closed by a galea and skin sutures of fine silk. A twenty-four hour drain was passed down to the dura at one spot because of some venous oozing.

The postoperative course was rather stormy. The temperature remained above normal for eight days, ranging from 101.6 to 102.4 F. For five days the patient's neck was stiff, and there was a suggestion of a Kernig sign. On the third day, about ½ ounce of blood-stained fluid was discharged from the right nostril, this recurred from time to time until the eleventh day when it ceased permanently.

By the thirteenth day there was a definite change in the mental status. He was oriented, had insight, fed himself and controlled his excretions. On the sixteenth day after operation x-ray examination did not show any evidence of pneumocephalus. There was no mental abnormality; the pyramidal signs on the right side had disappeared, except for slight diminution of the abdominal reflexes and absence of normal plantar flexion. Strength, coordination and gait were normal; odors were recognized; the optic disks were slightly pale, but the veins

were of normal size. The left facial paralysis was gone; the inequality of the palpebral fissures remained; there was no visible deformity of the bone in the frontal bone. The percussion note over the flap had the customary resonance of a flap, but nothing of the hollow drumlike quality present during the pneumocephalus remained. Over the rest of the skull the note was a normal, flat, high-pitched one.

Three months after operation, complete examination showed only slight pyramidal signs and slight disturbance of tactile discrimination in the right lower extremity. An x-ray picture did not show any evidence of air within the cranium. There were no subjective symptoms. The patient had been working regularly for two months.

Twenty-seven months after operation, in answer to a follow-up letter he wrote, "I am feeling fine; nothing bothers me whatever."

In his article, Dandy says, "It hardly seems possible to make an absolute diagnosis of pneumocephalus from any combination of signs and symptoms except one, sneezing followed by cerebrospinal rhinorrhea." Teachenor (*J. A. M. A.* **88**:987 [March 26] 1927) contends that the roentgenogram is the only method of diagnosis. In this case a positive diagnosis was made long before the roentgenograms were taken, and the deciding factor in establishing the diagnosis was an easily elicited physical sign, namely, the extraordinarily resonant percussion note of the skull. Jean and Villechaise also noted this sign in their case. In every instance of pneumocephalus, carèful examination of the skull by percussion should reveal a characteristic change of the percussion note over the region of the brain in which there is a large collection of air.

Of the thirty-eight cases, twenty patients were operated on and six died, a 30 per cent fatality. Of the eighteen patients not operated on, seven died, a 39 per cent fatality. Several authors concluded that surgical intervention was not advisable, for it appeared that the patient had an equally good chance of recovery without it. On reviewing the operations in cases in which the entrance of air was due to a fracture of the frontal sinus, however, it was found that in only seven cases was a definite attempt made to shut off the communication between the air pocket and the sinus. Only one of the these seven died, (14 per cent), and the rest recovered promptly with minimum residual symptoms. In this type of case in which the point of entrance of the air is so seasily accessible, and in which there is presumption or proof that the air pocket is enlarging or stationary, any intelligent attempt to block the passage is justified.

Summary.—1. The report of a case of pneumocephalus is added to the thirty-seven already recorded in the literature. 2. A change in the percussion note of the skull is suggested as a diagnostic sign of this condition. 3. An attempt to correct the condition by operative procedure is justified in selected cases.

DISCUSSION

DR. BROMBERG: A young man, under the care of Dr. I. Strauss in the Mount Sinai Hospital a month ago, suffered a severe trauma to the head and was taken to the Fordham Hospital where he remained for three weeks. He was unconscious for several days, and immediately on regaining consciousness noticed a flow of clear fluid from the right nostril. This continued for two months up to the time he came to the Mount Sinai Hospital. An intranasal examination was not made because of fear of inducing meningitis. Definite evidence was not found of fracture, except the history of trauma and the coma which followed. The x-ray observations disclosed an enormous pneumatocele in the right hemisphere with air in the lateral, third and fourth ventricles. Dr. Strauss did not consider the case suitable for operation and treated the man by the simple device of keeping the head at complete rest for a period of three weeks. At that time the x-rays did not show air in the ventricles, and only a small amount in the cerebral hemispheres; four weeks later the patient was discharged from the hospital, was up and about and the x-rays were absolutely clear. On admission he had shown left-

sided signs similar to the ones in the case presented. He had disinclination to speak or do anything asked of him. At the present time he is working actively as a chauffeur and enjoys perfect health; there are no neurologic signs on the left side.

DR. ALLEN: It seemed extraordinary that so many of these people with fracture of the right frontal sinus and a pneumocephalus had such a similar clinical picture. Several of the x-rays showed a pneumatocele like ours, just as yours did. Dandy's and Bullock's cases showed it. Several of the cases Bullock reviewed almost fell into a syndrome. Many of these patients recovered without an operation. That was the reason that a good many people advised against it. And it was for that reason I specified carefully that only when the condition was progressive or stationary should operation be considered. If a patient seems to be improving, it would be sensible to delay surgical intervention.

Regular Meeting, April 10, 1928

WALTER M. KRAUS, M.D., *President, in the Chair*

MADAME DEJERINE-KLUMPKE, 1859-1927. DR. S. E. JELLIFFE.

French neurology and neurology the world over mourns the loss of a personality rich in character and in scientific achievement. Madame Dejerine, whose death occurred in November, 1927, was, in the words of Professor Roussy, "one of the most beautiful and greatest figures in contemporary neurology." Her memory is enshrined among those who shared the kindness and the greatness of this personality in the nature of her work. For the latter was performed with such thoroughness, such demand for accuracy, and opened up so much hitherto undiscovered knowledge of neurology that it must continue to bear fruit.

Mademoiselle Klumpke was born in San Francisco, in 1859, one of a family of sisters who distinguished themselves in fields of art and science. She was 11 years of age when the family went to Europe, to Germany, thence to Switzerland, where Mademoiselle Klumpke received her academic education. She proceeded to Paris for the opportunity to study medicine, an opportunity which was hard won. Vulpian, later her teacher, and the one who exerted a life-long influence on her scientific ideals and attainments, was opposed to the entrance of women into medicine. His objections were nevertheless overruled and Mademoiselle Klumpke was not only allowed, in company with a few more mature women, to avail herself of the medical course — with great precautions, to be sure, on the part of Vulpian — but step by step she won the place of first woman extern and then intern in the hospitals of Paris.

She early came into contact with Dejerine, both of them sharing the inspiration and training of Vulpian. After their marriage their work continued in closest association until his death in 1917. As a woman, Madame Dejerine was distinguished by a modest self-reserve, combined with a warmth and kindliness of nature which made her beloved as a wife and mother, as hostess and as ever-ready guide and teacher to the students. At the time of her death she was engaged, with Madame Sorrel-Dejerine, her daughter, and Dr. Sorrell, her son-in-law, in building up the foundation which she had established for the Faculty of Medicine in memory of Dejerine. This has taken the form of a laboratory, museum and library for the advancement of neurologic study, and is now located in the building of the pathologic department of the University, Gustav Roussy occupying the Chair.

To set forth any adequate review of Madame Dejerine's work in neurology would be to write the entire history of modern French neurology. It began with the Dejerines in their insistence on continuous serial sectioning of whole brain material. This fundamental attitude gave rise to the partnership work on the Anatomy of the Nervous System, in 1894, which stands as a monument to Madame

Dejerine's attitude toward anatomic science in the neurologic field. In this work may be found that organizing genius of her mind, its capacity for detail and its ingenuity in presentation. The anatomy of the nervous system at this time was in a chaotic state. The newer researches of Golgi, Cajal, Forel and His, and the entire reformulations which followed on the establishment of the neuron theory necessitated an entirely new approach and a more rigid elaboration of neural topography. This work accomplished this and more, and stands as the summit of many years of patient research. For it was as early as 1883, while still an extern in Vulpian's service, that Mademoiselle Klumpke published two remarkable studies, which have become classic, on the relation of radicular palsies of the brachial plexus and ocular disturbances which are now extensively quoted as the Klumpke type of radicular palsy of the brachial plexus.

Her thesis continued her studies of peripheral nerves, which had always interested her, and dealt with polyneuritis, in general, and the lead palsies and atrophies, in particular. Then, after she was married to Dejerine, a number of studies from the pathologic laboratory at the Bicêtre and at the Salpêtrière followed. Among the most outstanding of these were those of secondary degenerations following lesions of the cortex; the course and connections of the ruban de Reil; the red nucleus; aberrant fibers of the pyramidal tract, and the course of the cuneus fibers in the corpus callosum.

These found a systematic presentation in the well known anatomy of 1894, in a union of work of husband and wife such as has rarely been seen. An immense number of studies followed this monumental treatise. It seemed but the beginning of a series of fertile researches with such students as André Thomas, Jumentié, Roussy, Mouzon, Foix, Landau, Long, Nageote, Tournay, Lhermitte, Tinel, Barré, Cellier and others.

When the World War came she entered the field and was active among the wounded at the Salpêtrière and later at the Invalides. At this time the care of cerebral injuries was minutely studied, and the indications for surgical treatment of injuries to the spinal cord. The monumental work of Tinel on injuries of the peripheral nerve was a continuation of Madame Dejerine's work on the evolution of these situations.

Even the death of Professor Dejerine, in 1917, did not interrupt her work. In collaboration with her daughter and Cellier at the Invalides there came forth the remarkable study of para-osteopathies of spinal paraplegia, and with Regnard she described the sympathetic synesthesia of paraplegias and ocular disturbances due to lesions of the lower dorsal cord.

In 1920 came the establishment of the "Fondation Dejerine" which, with the co-operation of Madame Dejerine, assured to the Paris Faculty of Medicine a laboratory, museum and library consecrated to the furtherance of neurologic science. In the words of Professor Roussy in his eulogy to Madame Dejerine, this Foundation was created in memory of the forty years of labor consecrated by Jules Dejerine to scientific research in neurology and of the recognition and welcome accorded in France in a period when feminism was so decried, to the six children of John Gerard Klumpke and of Dorothea Matilda Tolle, his wife, of San Francisco, who found important facilities for advanced educational work in France in the Faculty of Medicine, of Sciences, the Beaux Arts and the National Conservatory of Music.

I cannot forego the mention of one incident in her career, also mentioned by Roussy in his eulogy. I had the rare privilege of visiting the Dejerines in their summer home near Berne. The swiftly flowing river Aar was at their door. A young woman not able to swim had ventured in and was about to drown when Dejerine, a strong powerful man, endeavored to save her. He too was threatened with drowning and Mme. Dejerine threw herself into the water, all clothed, and rescued both of them. Anyone who saw, as I saw many years later, the seething, foaming stream could realize the courage and capacity of this remarkable woman and could well understand the stamina that has given so much to neurology not only in France but to the world.

One can point with pride to many in this country whose work has been of outstanding value from their contacts with the Dejerine example. Spiller, of Philadelphia, is perhaps the earliest of the Dejerine pupils; Archambault, of Albany, another. The entire neurologic activity of America owes its thanks to the researches of this remarkable pair.

CASE HISTORY AND POSTMORTEM OBSERVATIONS OF AN UNUSUAL TUMOR OF THE BRAIN. DR. CHARLES A. MCKENDREE and DR. JAMES R. LISA (by invitation).

The following case is presented not only because of the unusual distribution of the lesions responsible for the clinical picture, but also because of the unusual nature of the new-growth responsible for the clinical signs and symptoms.

Clinical History.—The patient, of Italian parentage, aged 18, single, a clerk, was admitted to the City Hospital on Oct. 19, 1927, complaining of headache, paralysis of the right side of the face, deafness of the right ear, paralysis of the ocular muscles on the right, numbness of the right side of the face and pain in the left lower extremity. The first symptom appeared in July, 1925, and consisted of tinnitus in the right ear. The patient had been well prior to this. In July, 1925, he noted buzzing in the right ear with gradual diminution of hearing on that side. In January, 1926, the right eyelid began to droop and the patient saw double. The ocular disturbance became progressively worse until the date of admission, when he could not move the right eyeball or the right upper lid. In May, 1926, he first noted numbness of the right side of the face. In July, he experienced severe headache on the right side, accompanied by the gradual onset of pain in the right side of the face. He was admitted to the Mount Sinai Hospital in August, where a craniotomy was performed and tissue was removed for histologic examination. The headache was relieved by this procedure for a time, but has recently become severe. Some time after the operation, the patient noted that the left side of the face was pulled to the left. Since August, 1927, he has suffered severe pain in the entire left lower extremity. The past history was irrelevant except for the fact that in April, 1927, the patient suffered from vertigo, which was so marked that he was unable to walk; objects seemed to revolve but the direction could not be ascertained. The personal and family history were irrelevant.

Physical Examination.—The patient was much emaciated and presented marked flattening of the right side of the face with complete ptosis of the right upper eyelid. The gait was normal except for slight unsteadiness due to weakness. The equilibratory and nonequilibratory tests were all normally performed. Skilled acts were normally done. There was some dysarthria due to facial paralysis and some dysphonia. There were no abnormal involuntary movements. The deep and superficial reflexes were normal and equal in both upper and lower extremities. The muscle strength was fair in all groups. The muscular status was normal except for marked hypotonicity in the lower extremities. There was generalized wasting and atrophy of the right side of the face. There were no abnormal associated movements. Signs of meningeal irritation were absent.

The general sensory examination for touch acuity, touch discrimination, pain, temperature, vibration and muscle-tendon sensibility was normal except for the right side of the face. Stereognosis was normal.

An examination of the cranial nerves showed that there were no olfactory disturbances; the sense of smell could not be accurately determined because of intranasal pathology. The fields of vision were normal to rough tests; there was a pallor of both disks, the left being more pale than the right. In the opinion of the consulting ophthalmologist, this pallor was due to postneuritic atrophy. The pupils were unequal in size, the right 5 mm., the left 2.5 mm.; the right did not react to light, the left reacted normally. There was slight exophthalmos on the right. The left eye moved normally in all directions while the right eye had no movement in any direction. True nystagmus was not noted, but there were a few

nystagmoid jerks on the left in extreme positions. The left palpebral fissure was normal; the right was entirely closed because of complete ptosis. There was haziness of the cornea on the right. There was marked flattening of the right temporal fossa and the right side of the face. There was marked weakness of the masseter, temporal and pterygoid muscles on the right. There was numbness on the right side of the face with complete analgesia and anesthesia of the right trigeminal distribution to all forms of stimuli. There was complete right facial paralysis with loss of taste on the anterior two thirds of the tongue. There was deafness on the right with no vestibular reactions to stimulation on that side. The palate rose slightly on each side in phonation. The quality of the voice was somewhat nasal. Examination of the vocal cords did not reveal actual paralysis, but the tensor action was weak on each side. The spinal accessory nerve was normal. The tongue protruded in the midline and to each side normally and was not atrophied.

The systemic organs, including the tegumentary, glandular and cardiovascular, were normal. Examination of the lungs did not reveal any abnormality. Roentgenograms of the chest did not show any essential pathologic change. The abdomen was normal.

Examination of the skeletal system revealed deformity of an osteoplastic flap on the right side of the head. A roentgenogram of the skull showed signs of increased intracranial pressure; the entire vault was thin; the sella turcica showed no evidence of enlargement or destruction. Examination of the vertebral column and a roentgen-ray examination of the four extremities gave negative results except for periosteal thickening in the upper portion of the left femur.

The mental status, except for irritability and under-productivity, was normal.

The blood and spinal fluid serology was entirely normal. A blood count showed a moderate secondary anemia.

Summary of Observations.—(1) Pallor of both optic disks, left more than right; (2) ophthalmoplegia totalis on the right; (3) total paralysis of the right trigeminus nerve; (4) complete peripheral paralysis of the right facial nerve; (5) nerve deafness and loss of vestibular reactions on the right; (6) weakness of the palatal muscles with sluggishness of action of the vocal cord.

Diagnosis.—The clinical interpretation of the case was that we were dealing with a neoplasm at the base of the skull on the right side, which involved by multiple processes the second, third, fourth, fifth, sixth, seventh, eighth, ninth and tenth nerves. The nature of the tumor was unknown, but we had received a report of the histologic study of material removed at a previous operation which indicated the presence of a sympathoblastoma. The patient died Dec. 10, 1927, of bronchopneumonia.

Autopsy and Histologic Studies.—The autopsy was performed three hours after death. The pituitary gland was moderately enlarged and continuous with a large mass filling the right middle fossa, tightly adherent to the basal dura. The mass had extended over the basal dura into the posterior fossa and the foramen magnum on the right side. The cranial nerves from the third posteriorly were involved in the masses which followed along their course through the emergent foramens. At the site of previous operation the inner surface of the dura was studded with small, hard, white nodules. Similar nodules, about the size of a pea, were present on the upper and lower surface on the right half of the tentorium cerebelli. The remainder of the brain was normal. In the lungs there were innumerable small, hard, white masses the size of a pea which had a distribution paralleling tubercles in acute miliary tuberculosis. The bronchial lymph lobes were enlarged and firm; on section their peripheries were filled by solid, opaque white masses. The remainder of the autopsy was entirely negative for the presence of any other tumor.

The microscopy was performed on areas from the pituitary gland, the mass in the middle fossa, the dura, the fifth nerve and bronchial lymph nodes. The striking feature of the majority of the sections was the reaction of the connective

tissue. In the pituitary glands the cell nests of malignant cells contained a few normal eosinophilic and neutrophilic pituitary cells. The peripheral lymphatics of the fifth nerve were distended by tumor cells. In the lungs and bronchial lymph nodes the reaction of the connective tissue was absent.

The diagnosis made was scirrhus carcinoma of the pituitary gland metastasizing to the lungs and bronchial lymph nodes.

DISCUSSION

DR. PERCIVAL BAILEY: On the basis of probabilities, the tumor arose in the lungs and metastasized to the brain, which is far more frequent. Naturally, one should not diagnose a condition on the basis of probabilities alone. However, that should be taken into consideration. Recently, there have been appearing reports of gliomas of the brain which have metastasized to the body; my interest was aroused by these reports and I sent for sections. One happened to be a typical melanotic sarcoma. Where it arose I do not know, but probably not primarily in the brain. In another case, of which I secured sections, both Dr. Mallory and Dr. Wolbach decided it was probably not a primary tumor of the brain, and I agree with them, although its exact nature is doubtful.

So, on the basis of probabilities, I should think the tumor was probably not primarily intracranial. I have seen two or three tumors similar to this which appeared to arise from near the hypophysis. In one, there were nodules also in the liver. I was never sure that the small nodules in the liver might not have been the primary lesion, and the larger intracranial tumor a metastasis from it. The primary tumor may be smaller than the metastasis.

That this tumor was a carcinoma, I think I will agree without having seen the sections themselves.

DR. GLOBUS: A diagnosis of sympathoblastoma has been reported. I was responsible for this diagnosis. It is most likely, from what was shown here tonight, that a part of the gasserian ganglion was removed at the operation and was responsible for the diagnosis of sympathoblastoma. I still have that section and am still of the opinion that the cells are sympathetic nerve cells, and in view of the fact that the surgeon reported removal of part of a tumor the diagnosis of sympathoblastoma was the most logical.

I agree with Dr. Bailey that carcinomas in the brain are most likely metastatic.

Some of you will recall a series of twelve cases which I have reported, in which the symptoms were strictly those of a lesion of the brain, and only after a thorough search was a primary focus found elsewhere. In this case it is most likely that the malignant tumor arose in the lungs and metastasized to the brain.

DR. RICHARD BRICKNER: Was anything found to account for the pain in the leg? Was a tumor found there, particularly?

DR. MCKENDREE: The only explanation for the pain in the leg was the periosteal thickening in the upper portion of the left femur that was found by the x-ray examination. We were not able to determine any other lesion.

DR. JAMES R. LISA: In regard to the observations in this case, to my mind it was not primarily tumor of the lung. The observations in the lung were those of multiple metastases. The other organs failed to show any site of a primary tumor. The examination was thorough and, because we knew the previous history and the previous diagnosis made in this case, we made a careful examination of every organ in the body and found nothing except what has been previously mentioned.

SOME UNUSUAL TUMORS OF THE THIRD VENTRICLE. DR. PERCIVAL BAILEY.

In Boston, tumors of the brain are not always well diagnosed nor well examined pathologically. They are often well operated on by Dr. Harvey Cushing. A few of these cases I will present this evening. I fear the remarks I have to make will not prove excessively interesting, but my interest in this

subject was aroused by the entrance of a woman, aged 23, into the clinic of Dr. Harvey Cushing complaining that she fell asleep in inopportune places and at inappropriate moments. She was a school teacher and had charge of the sixth grade in a public school; she would fall asleep suddenly during the class and was obliged to resign her position. Some six years before she had had an attack of febrile jaundice, which was thought to be due to malaria. The jaundice had disappeared, and she had developed these attacks of sleepiness. The attacks were accompanied by weakness of the knees and were usually brought on by exertion or excitement; they were followed by periods of depression in which she wept and felt out of sorts. Headaches finally accompanied the attacks, and it was for that reason she was sent to the hospital. We found none of the general symptoms of tumor of the brain.

The spinal fluid tension was normal. The patient was adipose, having gained about 40 pounds in weight. She had a delicate skin. The menses were irregular. She had a slight polyuria. The basal metabolic rate was not examined.

I had never seen so clearcut a case of what is described in the literature as narcolepsy. With Dr. John Fulton I endeavored to find out something about this disease. It was described by Gelineau some years ago. Adie decided that some lesion in the basal region of the brain must be associated with this syndrome. The few slight general constitutional symptoms of the patient caused us to investigate tumors which had been observed in the clinic to see if something similar could not be found.

CASE 1.—The first patient had attacks which, in the early part of the disease, resembled closely those of the previous patient. She was 28 years of age when she entered the clinic. She was almost constantly somnolent. She could be aroused to take meals, otherwise she fell asleep and slept practically continuously. She gave a story of having begun to fall asleep six years previously, two years after the birth of her first child. She had been accustomed to play pinochle with her husband and usually won; she now found that she was losing because she fell asleep in the middle of the game. Shortly afterward she began to fall alseep when visitors came. Soon after these attacks she began to have polyuria. She was not conscious of great thirst, although she remembered that she drank excessively at that time. The symptoms continued and at the height of the polyuria she was drinking 5 or 6 gallons of water daily and was excreting the same amount of urine.

About three years after the polyuria and the sleeping attacks began headache occurred, but it was never a prominent symptom. From the onset there was remarkable fluctuation in weight. She weighed about 138 pounds (62.6 Kg.) when the illness began; six months later she weighed 120 pounds (54.5 Kg.). Then, gradually, she began to gain so that she was over 200 pounds (90.7 Kg.) when she entered the clinic. The menses had stopped completely and had not returned, although she had had severe pain radiating over the abdomen and recurring at regular monthly intervals.

She was very adipose, sleepy, stupid, somnolent and half comatose; the pubic and axillary hair was gone. She could hardly be aroused to have a picture taken. She had primary optic atrophy in both eyes with bitemporal hemianopia to rough test. She had no polyuria when she was in the hospital.

She said that when she was so much annoyed by the polyuria she was placed on a certain dietary regimen in which nuts figured largely and meat was forbidden. Two weeks after beginning this diet the polyuria disappeared, never to return. Aside from the primary atrophy in both eyes, little was found. The sella turcica was normal. A subtemporal decompression was performed as we were unable to locate the tumor. That was some years ago. One might suspect its localization today; its nature, however, would be difficult to diagnose even today. The patient died of hyperthermia. At a necropsy, limited to the brain, a small firm vascular tumor was found in the hypothalamus. The stalk of the pituitary body was normal. The pituitary body was normal in size. There was no internal hydrocephalus. In the stalk of the hypophysis, and in the optic chasm practically

all nerve fibers had disappeared. The whole tuber cinereum and hypothalamic region was involved by the tumor.

A reconstruction made from median sections showed the extent of the tumor. Not all of the tissues in this region were destroyed by the tumor. It had infiltrated along the vessels, leaving the hypophysis entirely free.

Microscopically, the tumor proved to be made up of small round cells, in which mitotic figures were fairly numerous. Some of the cells were multinucleated; some showed what might be interpreted as amitotic division. These cells were enclosed in a reticulum of connective tissue, which had a tendency to whirl around the blood vessels as is often found in sarcoma.

The anterior part of the hypophysis showed normal distribution of the chromophil cells. The posterior lobe was normal. A little cyst, such as is usually found in the pars intermedia, was present.

This tumor was microscopically, I think, a sarcoma, that is to say, a malignant round cell tumor of mesodermal origin. Whether it was primary in the brain or not I am not prepared to say, because a complete necropsy was not done. There were no clinical signs of tumor elsewhere in the body.

The case was interesting from the onset. One might have regarded it as a typical case of narcolepsy had it not been for the intense polyuria. Furthermore, the menses had stopped early. The intensity of the polyuria and the cessation of the menses might have made one think that it was not an essential narcolepsy.

I will call attention to the presence of a complete adiposogenital syndrome without involvement of the hypophysis. Perhaps the secretion of the hypophysis was shut off, but if so there was no evidence to be found in the histologic examination of the hypophysis itself. The patient had a complete syndrome, with diabetes insipidus and narcolepsy, from a small tumor which had not caused internal hydrocephalus, and probably not increased intracranial tension.

In the absence of general symptoms of a tumor the patient had narcoleptic attacks early. The early syndromes in cases of tumor of the brain are those of importance from a localizing standpoint. It seems that this tumor confirms the idea, expressed by Adie, that perhaps a lesion in the third ventricle or the diencephalic portion of the brain is responsible for these narcoleptic attacks.

Case 2.—A man, aged 38, had always been well until suddenly, one day in 1924, he fell ill with severe headache and vertigo. In 1926, he had a similar attack in which he slept continuously for a day and a half. Other attacks of severe headaches occurred, in which he was uncomfortable and vomited, but he never had another sleepy attack.

Little was found on examination except choked disks and vague cerebellar symptoms. A ventriculogram showed that the third ventricle did not fill, but little attention was paid to that because ventricular injections sometimes do not fill the third ventricle. A suboccipital exploration was done. Probably the most frequent error made in a neurosurgical clinic is to operate on the cerebellum for a tumor in the region of the third ventricle. Some thickening of the arachnoid was found around the cerebellum. The man recovered rapidly and was discharged from the hospital, apparently relieved. He went home and a short time afterward his physician called to say that he was having an attack. A lumbar puncture was suggested and performed, but the patient died from a pontile hemorrhage.

We secured an examination of the brain and were greatly surprised to find this small round tumor, about the consistency of a rubber ball, sitting in the third ventricle, which was scarcely dilated, attached anteriorly and free behind. There was a certain degree of internal hydrocephalus. A search of the literature revealed some twelve or fifteen such tumors described under all kinds of names and in odd places. Inside the tumor was a mass of colloid material without structure, and around it a cuboidal epithelium with some tufts of choroid plexus on the lower surface. Descriptions of other similar cases show practically the same thing, a cyst filled with colloid material which, after fixation, becomes about the consistency of a rubber ball.

These patients have sudden severe periods of headache. The patient may be doing his work and develop severe headache, lie unconscious for three hours and then recover, only to have the same thing recur. Finally, in one of these headaches he will die.

Most of these tumors have been recorded in the Scandinavian literature. Sjövall, in Sweden, supposed that the tumor might be a remnant of the paraphysis. In the human embryo this organ is rudimentary, and it disappears early. The point of attachment of these tumors makes the hypothesis of Sjövall seem to be reasonable.

CASE 3.—This patient also had a tumor confined to the third ventricle. He was a young man who, while doing college work, began to have severe headaches. He had attacks from which he would recover and go about his business. He was drowsy and was thought to have epidemic encephalitis. He soon showed emotional indifference, sometimes like that of a patient with dementia praecox. A left osteoplastic exploration had been performed in New York. We performed a suboccipital exploration. Finally, the tumor was located in the third ventricle and an attempt was made to remove it by going through the right hemisphere. There was a huge internal hydrocephalus and the tumor was seen but could not be removed. It filled the entire third ventricle with the exception of the infundibulum and was not attached anywhere except to the right column of the fornix. I interpret it as a glioma of the type known as an astroblastoma.

CASE 4.—A boy, aged about 15, an Italian, came first to the Massachusetts General Hospital complaining of constipation. He was given some pills and advised to come back the next day and bring a twenty-four hour specimen of urine. He came back with 3 gallons. He entered the Boston City Hospital where a lumbar puncture was done and yielded practically normal results. Efforts were made to suppress the polyuria with pituitary, but he insisted on being discharged and came to the Brigham Hospital.

On admission he was rather undersized, but otherwise fairly normal. Aside from slight emaciation and polyuria nothing was found. Since the polyuria was not stopped by pituitary, it was thought at the clinic that he had a psychoneurosis. I had seen a patient showing similar symptoms who had a tumor in the third ventricle and I proposed making a ventriculogram; this was refused and he was discharged. He then went to the Massachusetts Hospital; here he developed swelling in the parotid glands which was thought at first to be mumps, but was later regarded as angioneurotic edema. He had then an abnormal spinal fluid but no diagnosis was made. At this time he also presented mental symptoms and he was transferred to the department of abnormal psychology of Harvard University. There it was decided that the water drinking was a compulsion neurosis.

The boy was one of a large family; the father was a barber, a dominating person; the mother was a submissive person, but an interminable talker. The father thought the mother was the most aggravating person of his acquaintance. When he could stand her chatter no longer he used to beat her. The boy took his mother's part and used to battle with the father. He used to help his mother with the household work. One of his earliest recollections is going to the well to bring water for his mother; while there he was beaten by a rival gang. He remembered that afterward he went to the well and drank copiously of the water. His mother had taught him that drinking water was the best way to get rid of fear. After the beating he continued to drink copiously of water; that was the onset of his polyuria. After he had been in the Brigham Hospital he became well, for his father was sent to Deer Island for beating his wife. Later, a policeman gave the boy a beating, after which the polyuria began again; but later, he improved, but the condition began again with an acute exacerbation when the father left Deer Island.

The polydipsia was therefore thought to be a compulsion having something to do with his fears. He was sent away from the family to the country and he continued to do very well there for a time; later, he began to fall asleep in the

course of the day and could not be roused. He complained also that he could not see well. The mother brought him to the hospital, apparently in extremis. He was sluggish; the pulse rate was slow. When Dr. Cushing arrived he was sitting up in bed talking and laughing with the nurse. At 5 o'clock he was found dead in bed.

At necropsy there was found a large tumor filling the third ventricle. The pituitary body was not involved. The tumor was disseminated all over the lateral walls of the ventricle. The tumor proved to be a pinealoma.

The polyuria was due to involvement of the tuberian region, as happens frequently with pinealomas. It may be that when he had his fight with the rival gang, part of this tumor was broken off and lodged in the infundibulum giving rise to polyuria.

DISCUSSION

DR. GLOBUS: Perhaps I may stress the point that tumors in the region of the third ventricle are most difficult to diagnose, not only clinically, but also anatomically. It is there that one finds the greatest variety in the histologic make-up of tumors, and surprises are found particularly in tumors arising in that region. Even tumors of the same variety show such variation that it may be said that there are no two tumors within or about the third ventricle which are exactly alike in the gross or histologic make-up.

The cases presented by Dr. Bailey are also of interest because they emphasize once more the physiologic significance of the structures in the region of the third ventricle. During recent years stress has been laid on the presence of centers in the structures about the third ventricle in the control of vegetative functions.

DR. KRAUS: The introduction of the question of narcolepsy interests me greatly. My first experience with this condition was in 1915, when I saw a fat man who had been deprived of his chauffeur's license because he had fallen asleep while driving a truck and had driven it into a beer saloon. That man had a large sella turcica. I did not see his brain at autopsy, but probably it would have been better if I had, because as far as I know the only thing he succeeded in doing while I had him under observation at Bellevue was to sleep all day long in the yard. At that time, I read Gelineau's original paper and became somewhat interested in the subject.

Recently, Lhermitte and Tournay sent me a review they read before the Neurological Society of Paris on the question of sleep. It is extremely thorough and these problems are discussed among others. Pawlow showed that a conditioned inhibition will produce sleep in a dog. It may be of interest to know that it troubled Pawlow in his earlier experiments to find that his dogs would go to sleep without his wishing them to. He ultimately came to the thesis, which he proved abundantly by subsequent work, that the mechanism of sleep had to do with progressive inhibition of the cortex.

What I wish to emphasize is that one school requires the cortex for the mechanism of sleep and states that any disorder of the cortex of the nature of inhibition, if widely enough spread, will produce sleep; another school has shown that tumors in the region of the third ventricle will frequently produce narcolepsy and other forms of sleep. The problem, therefore, that presents itself to me is, have I ever seen a neoplasm of the cortex that produced narcolepsy? My reply is "no." Therefore, I come to an important conclusion, which Dr. Bailey's paper brings to mind, namely, that when one finds an abnormal state of sleep like narcolepsy one is probably confronted in almost every case with disease about the floor of the third ventricle, and not with the disease of the cortex.

A third point of view was brought forth at the Research Society last Christmas. Dr. Louis Stephenson and Dr. Wortes have shown at Bellevue that increased intracranial pressure has a definite relation to sleep. They showed this by drug actions, a description of which I shall omit. One knows that increased intracranial pressure is frequent in tumors of the brain whether of the third ventricle or more posterior. Yet one does not have narcolepsy universally or frequently in those

types of tumors. Consequently, there is a third point of view to consider. One has to consider disorders of a normal sleep mechanism of the cortex, disorders of a normal sleep mechanism in the region of the third ventricle, and disorders of a normal sleep mechanism by a change of intracranial pressure. One might assume that this would affect the region at the base of the third ventricle.

DR. SACHS: The points of special interest that I felt in the whole discussion included (1) the principle, which does not seem to be always borne in mind, that even when there is not distinct anatomic change or distinct interference with the structure of the brain there may be distinct interference with physiologic function. If one finds, for instance, on making a section that there is no involvement of the tuber cinereum in a certain case, that does not prove that that tuber cinereum has not been interfered with. Physiologically, it probably was interfered with distinctly, even if there was no anatomic involvement.

(2) I cannot help thinking that these cases are of importance in and that they certainly help to explain, for instance, the lethargy—the drowsiness and sleepiness —that occurs in epidemic encephalitis. I have no doubt that in those cases the encephalitis gradually involves the hypothalamic region. Many cases of encephalitis are restricted largely to that special region.

DR. JELLIFFE: The whole group of problems connected with narcolepsy, hypnolepsy, pyknolepsy or any other name that may be given to it—catalepsy, epilepsy, etc.—are so closely interwoven that to insist on "names" as standing for things rather than understanding the process that is going on does not get one very far. Lethargy as an outstanding symptom in encephalitis offers a great number of clews, reaching out in a great number of directions. Two months ago I had the pleasure of trying to tell you something about the relationships of the diencephalic synapses or nuclei to other connections within the central nervous system. Until Dr. Bailey gives one not only cellular studies of all of the diencephalic nuclei, but also the interruptions that have taken place in the various fiber tracts, such as between the tuber cinereum and the thalamic structures, the corpora mamillaria and the various other nuclei, the degenerations or interruptions in the tractus hypophyseus of Pines—in other words, until one knows more about the interruptions in the mechanics of the in-sweeping series of stimuli from not only the external environment but also from the visceral environment, one will be in the dark; so far as the brain is concerned the viscera are environment. The whole somesthetic series of stimuli as they sweep up, first into the diencephalic structures, including the larger ones of the thalamus, have to be more carefully analyzed from the standpoint of interruption of stimuli that after all determine vigilance, or awareness, or being awake. So much for the anatomic situation.

It is quite compatible with what one knows that tumors of the tuber cinereum, and other tumors in the region of the third ventricle (where Economo puts his hypothetical sleep "center"), would impinge sufficiently on the incoming stimuli so that vigilance will not be maintained.

The first patient with narcolepsy I saw, about fifteen years ago, was brought to me by a surgeon. He had removed part of her intestine, a large part of the uterus and part of the ovaries; I believe that her eye muscles also had been cut. I listened nearly two hours to the story. I then told him that in my opinion the narcolepsy was a masturbatory equivalent. He imparted some of the information to the patient, who wrote me an indigant letter. After a year she came in without the surgeon and went over the story again. She told me what he had told her. I told her I had not changed my mind concerning the whole train of events, which were somewhat similar to what Dr. Kraus has described, but that I felt there were many other things with the narcoleptic picture that had not been mentioned. I told her I still thought that it was the equivalent of masturbatory activity and she again became angry and left. A year later she came in and apologized. She said that only two days before she had concluded, after having three or four of these attacks, that possibly there might be something in what I said. She therefore decided to masturbate consciously and the whole series of phenomena took place immediately.

Many of you smiled when Dr. Bailey spoke of the neurosis theory concerning the Italian barber's son, but I can assure you that from the writings of Greving, Goldstein, Stern, Kleish, Nachmanson, Schilder, and many other observers, it will be seen that one is justified in seeking the kernel of compulsion neuroses in the diencephalic involvements of encephalitis. In 1919, Vogt said that involvements of the striatum almost invariably increase the capacity for suggestibility. He even said that, in his opinion, some day the anatomic substratum of hysterical hypersuggestibility will be found in striatal lesions. Although that is entirely too dogmatic and too narrow a presentation of the situation, it seems to me to contain a great deal of truth, although it dodges the psychologic level issues.

Polyuria is found not infrequently in narcoleptic cases; in postencephalitic narcoleptic cases it is frequent. Just which or how many diencephalic fiber tracts must be involved it is not yet known. Some studies have shown that the regulation of sugar metabolism, of salt metabolism and of calcium metabolism is dependent on the integrity of the diencephalic coordinating structures.

DR. WECHSLER: The cases shown by Dr. Bailey are of importance because they bear on the syndrome of the third ventricle. I fear that in general there is too glib a tendency to make syndromes of the third ventricle. Dr. Weisenburg, many years ago, described what he thought was such a syndrome, characterized essentially by ataxia and disturbances of upward gaze. Actually it is difficult to conceive of a syndrome peculiar to a space, such as the third ventricle; in fact, there is not a definite one any more than there is a syndrome of the fourth or lateral ventricles. The symptomatology depends essentially on involvement of adjacent structures. From my reading of the literature on tumors of the various ventricles I have been unable to come to the conclusion that there is any definite syndrome pertaining to the various ventricles.

That the hypothalamus is frequently involved can be explained by the fact that it is close to the third ventricle. In the cases shown here, however, the absence of choked disk speaks rather against obstruction and consequent internal hydrocephalus.

The question of a sleep center, it seems to me, is also one that is too readily decided. The evidence so far presented does not convince one that there is one sleep center. There is a tendency among neurologists to speak too strictly of brain centers. That the particular region in question has to do with sleep is evidenced from encephalitis, from tumors and from other lesions, but to say that it is the sleep center is not as yet justified. Sleep is perhaps best considered as a function of the entire organism. There are at least half a dozen causes of sleep: toxic conditions, anemia of the brain, hyperemia, compression and other conditions. Whether the periodicity of sleep has to do with the center I do not know. For a long time it was thought to be due to dysfunction of the hypophysis. One might speak of this region as a region which in some way has to do with sleep. Even so, these patients did not show true sleep; they lack the essential characteristic of sleep, which differentiates it from coma, namely, the ability always to be aroused.

DR. BAILEY: It was perhaps a little malicious on my part merely to present four cases. I might have described many syndromes of the third ventricle, but I was careful not to say anything about a syndrome of the third ventricle. I was also careful not to speak about a sleep "center." In these four cases the correct diagnosis was not made or was made late. I would never attempt to make a diagnosis of tumor of the third ventricle on the symptom of somnolence alone. After all, a single symptom on which one may base a diagnosis is rare. Diagnosis is usually made from considering all the symptoms and looking at them from every possible standpoint to find how they can most reasonably be fitted together. If a patient came to me with an attack of narcolepsy and I could find no other symptom, I would make a diagnosis of narcolepsy, and put the patient under observation with the possibility in mind that he might develop other symptoms in this neighborhood.

I have never observed attacks of narcolepsy or attacks which resembled narcolepsy except in cases of tumor at the base of the brain, either in the hypophysis or in the region of the third ventricle. Most patients with tumor of the brain are more or less somnolent, torpid and stuporous and show pathologic disturbances of sleep. It is not reasonable to expect that a pathologic disturbance of sleep which is produced by an organic lesion of the brain should be normal sleep. It will show more or less relationship to sleep, but will not be normal.

The first patient of whom I spoke had symptoms in the beginning which resembled closely normal sleep, because she was easily aroused. Her husband had only to poke her in the ribs with his elbow and she woke up.

Tumors of the brain are not good subjects on which to base a study of the localization of function in the brain; they produce too widespread generalized symptoms. Case 1, however, seem to me as good a subject for a localization study as a tumor of the brain can possibly be; though the lesion was localized and destructive it had not given rise to internal hydrocephalus. Therefore, it seems to me that the symptoms which the patient presented must have been due to a lesion in the particular region destroyed by the tumor or somewhere near the region.

VENOUS DILATATIONS AND OTHER INTRASPINAL VESSEL ALTERATIONS, INCLUDING TRUE ANGIOMAS, WITH SIGNS AND SYMPTOMS OF COMPRESSION OF THE CORD. DR. J. H. GLOBUS and DR. L. J. DOSHAY,

Four patients in whom circumscribed conglomerations of dilated veins of the spinal cord were associated with signs and symptoms of compression of the spinal cord were presented with a description of the postmortem observations in one instance. The literature on the subject, containing twenty similar cases, was reviewed. Under the term dilatation of spinal veins were assembled all those instances which have been variously described under such titles as spinal hemorrhoids, cirsoid aneurysms of the spinal veins, varicose dilatations of the spinal veins, angioma venosum racemosum and simple angiomas. It was pointed out that, while this form of spinal vessel alteration is considered rare by many, there is evidence that it is more common than is generally believed. It was suggested that among the factors involving the production of this type of vessel alteration there is a preexisting or concomitant change in the involved veins in the nature of an inflammatory or degenerative process. This is usually coupled with some other factor which causes compression by intensive muscular exercise or abnormal posture of some part of the venous channel so as to impede the return of the blood flow.

The anatomic observations in one case were: marked varicose dilatation of the dorsal pial veins, with extension of the process to the vessels of the spinal cord; degenerative changes in the arteries and veins in the nature of moderate arteriosclerosis and phlebosclerosis; marked disorganization and disintegration of the substance of the spinal cord.

The condition is rarely recognized clinically since the subjective manifestations and objective observations are mainly those of compression of the spinal cord, and a diagnosis of tumor of the spinal cord is commonly made. An analysis of the clinical features in the group of cases did not reveal any signs or symptoms which could aid in the clinical identification of the true character of the lesion. They differ somewhat from neoplasms of the spinal cord by the atypical manifestations of compression and involvement of the cord, including signs pointing to dissemination of the lesion and to invasion of the cord, and by the absence of subarachnoid block. Given a case with signs and symptoms of compression of the cord, with or without features of direct involvement, with no demonstrable subarachnoid block in a person in late adult life, venous dilatation of intraspinal vessels may be considered among and alongside of other diagnostic possibilities. In any event an exploratory laminectomy is indicated. It is, however, necessary to bear in mind that instances are not infrequent in which the substance of the spinal cord

is invaded by these dilated vessels and has undergone degenerative changes. Hence, if laminectomy discloses dilated veins on the surface of the cord, thorough investigation of the spinal canal is required first to exclude the possible existence of a neoplasm of the cord at a somewhat higher level and to make certain that there is no extension of the lesion into the substance of the cord. If the latter is found, laminectomy and decompression is all that should be undertaken; more radical steps, such as removal or partial resection of the vessels, may lead to a fatal termination; decompression is not unlikely to give satisfactory results.

Alongside of these cases in which only venous dilatations were found, a group of arterial or arteriovenous aneurysms of the spinal vessels were described. They, however, did not vary clinically from the previous group.

In a third group there were assembled only cases in which the term hemangioma was justified by the anatomic features. The terms "'angioma and hemangioma" were restricted to true vascular tumors, in spite of the common practice of including incorrectly under the term "angioma" conditions which are best described under the name "venous dilatations." The existing confusion prompted a survey of instances of true hemangioma. It was thought highly desirable to differentiate these two conditions (venous dilatations and angiomas) and put an end to the chaotic classification of such material. The hemangiomas were subgrouped into intramedullary, extramedullary (pial), epidural and vertebral hemangioma. Of this group the epidural hemangiomas were the more numerous and were particularly interesting since, because of their location and character, they benefit by surgical intervention. Clinically, the hemangiomas, unlike the venous dilatations, give rise to discrete signs of cord compression.

The roentgen ray is of service since it helps to distinguish vertebral hemangiomas, which cause rarefaction of bone, from dural hemangiomas.

DISCUSSION

DR. SACHS: I have often thought that it was too bad the circulation of the spinal cord has not been studied and followed as closely as has irregularity of the circulation of the brain. The various types and the difficulties of diagnosis were correctly accentuated. I wish to stress one point because it has distinct practical value; it is well, particularly in elderly persons, to bear in mind the irregularities of the circulation of the spinal cord, and not to arrive too hastily at a diagnosis of tumor of the cord. Within the last ten years I recall observing a number of persons of the ages of 55 or 60, who have complained of mild paralytic symptoms, mild disturbances of sensation and interference with the vesical and sometimes the rectal reflexes, and have presented such symptoms as would ordinarily lead to a diagnosis of a transverse myelitis or something akin to that. Such disturbances are extremely frequent in elderly persons, and if one will study not only the symptoms of the spinal cord but also the circulation of the extremities, I think one will often find reason to reflect whether or not such symptoms are due to neoplasm of the spinal cord. Some of the patients to whom I referred I have rescued from operation; in several of the cases improvement followed without operation. If there is one type of symptoms or if there are any signs that might help one to differentiate between spinal neoplasm and these vascular conditions, it is that none of the symptoms are as complete as one would expect to find nor as progressive as they would be in cases of spinal neoplasm. The paralysis seldom becomes complete. It is not always symmetrical. The disturbance of the bladder is of the type often observed in elderly persons. The thing that strikes me particularly is that the sensory symptoms are never marked. They are of the sort for which one has to hunt. While one may in some of these cases even find "level lesions," the actual degree of involvement of the sensory system is extremely slight, and the point that has always impressed me is that the symptoms do not take on a progressive character.

The substance of the spinal cord is, I think, interfered with much more seriously by irregularities in the capillary blood supply than it is by vascular

dilatations that are seen on the surface of the cord. I must leave it to surgeons to determine whether these are proper cases for surgical manipulation, although Dr. Globus said four of ten cases were successfully treated. I think that, in elderly persons when these doubtful symptoms of neoplasm appear, it would be wise not to attempt much in the way of surgical intervention unless one can prove by injections of iodized oil 40 per cent that there is a distinct block. I have seen at least two vascular cases in patients under the age of 40; but these cases are particularly frequent in elderly persons.

DR. ELSBERG: During the past few years several articles have been published on the subject of abnormalities of the spinal veins and spinal hemangiomas. In them were included, under one heading, a number of different conditions, and I am glad that Dr. Globus and Dr. Doshay have made a clear distinction between cases in which there are only enlarged varicose veins on the surface of the cord or within its substance and cases in which there is an actual tumor which histologically is found to consist of a mass of blood vessels.

A number of years ago, before finer tests for the determination of a subarachnoid block were available, not a few patients were subjected to operative intervention who would not be operated on today. A number of years ago, when exploratory laminectomy was performed more often, I saw many instances of abnormalities of the spinal vessels, many more than will be seen today. I believe that one can group the patients in the following way: (1) Those who have enlarged, varicose veins on the surface of the cord either over a localized area or along the entire length of the cord. In these patients there is usually no subarachnoid block and the symptoms are frequently rather vague and diffuse. (2) Those cases in which there is a marked enlargement of the vessels on the surface of the spinal cord secondary to a tumor which compresses the cord at a higher level. (3) Those patients who have a strictly localized mass of vessels either on the surface of the spinal cord or both on its surface and within its substance. In these patients there may be definite level symptoms, although one can never say with certainty whether the symptoms are due to compression or to compression and involvement of the cord itself. (4) Those cases in which there is a localized mass of vessels on the surface of the cord between the roots of the cauda equina. In these patients the prominent symptoms are radicular in character, although they may have signs of cord or root compression. In a number of instances I have excised these varicose veins either at some level in the cord or between the roots of the cauda equina. If such a localized mass of varicose veins is found at operation and there is no involvement of blood vessels within the substance of the cord, the cases are suitable for radical surgical extirpation. (5) Cases in which there is a tumor which at operation is not considered to be made up of blood vessels, but in which microscopic study shows a mass of blood vessels within a well defined capsule. It is still an open question whether these true tumors of the spinal cord are not meningeal fibroblastomas with marked development of blood vessels or whether they are true angiomas or hemangiomas. In two patients, in my personal experience, the growths were extradural, and the tumors that were removed were supposed to be extradural meningiomas until the report from the laboratory showed that the tumor was an hemangioma. This fifth group of cases should be kept strictly separate from all other abnormalities of the spinal vessels, because in this group one is dealing with a true tumor formation.

DR. BAILEY: This presentation is gratifying to me because Dr. Cushing and I have just completed a monograph on vascular tumors of the brain. Probably we should have waited until after I came here this evening. We also tried to point out that they should be divided into vascular anomalies and true tumors, and tried to distinguish between them. I believe there are true angioblastomas, not only in the nervous system but also in the spinal cord.

My belief is strengthened by a monograph which appeared a year or so ago from the University of Lund, in which the author developed at great length the association of angioblastic tumors in the retina, angioblastomas of the cerebellum

and angioblastomas in the spinal cord, these being associated with cystic kidneys, hemangioma of the liver, tumors of the epididymis, and other tumor formations, the whole constituting a widespread tumor formation of the mesoderm which is now being referred to in German literature as Lindau's disease. Lindau's report caused us to restudy our patients and we found that one had an angioma of the retina. Furthermore, the father of this patient had died of a cyst of the brain, so that this disease complex, which seems to be just as definite as von Recklinghausen's disease, is probably not infrequent.

DR. GLOBUS: I will show one more picture. This is one of a vertebral angioma associated with a dural angioma, in which the dural angioma was the one that was responsible for the symptoms of the spinal cord.

Book Reviews

DIE ANGIOARCHITEKTONIK DER GROSSHIRNRINDE. By RICHARD PFEIFER. Pp. 157, with 130 illustrations and 2 plates. Berlin: Julius Springer, 1928.

This book represents a great deal of careful work in a new field. It is well written, the illustrations are splendid and the general plan and execution are good. The literature on cerebral vascular injection is carefully reviewed from the time of Vicq d'Azyr, 1878, to the present and the technic of each author is criticized. The main trouble with all previous work was that the injection of the arterioles, venules and capillaries was incomplete; this gave a false picture and led to erroneous conclusions as to physiology and pathology. The author, therefore, has developed a technic which gives complete injections of all the vessels. Moreover, he describes at length his method of determining whether or not a preparation is completely injected. This is done by tracing complete vascular loops with an Abbé drawing apparatus; for general study the stereoscopic microscope is most useful. The sections are always thick, often as much as 100 microns; so complete capillary loops may be seen by focussing up and down. The painstaking drawings made with the Abbé apparatus are admirable, especially the two large folding plates at the back of the book; one of these shows the ramifications of an artery in a section of the rhinencephalon of the cat; the other is similar, showing the ramifications of a vein in a section from the gyrus lateralis of the cat's cortex. These are beautiful and unique in their clear demonstration of the anatomy.

The principle conclusion drawn from this work on the cat is that the cerebral vessels form a *"Kontinuum,"* a truly endless net; there are no "end-arteries" in the brain, in Cohnheim's sense. This is important and the proof is convincing. The author states: "If one imagines a red blood corpuscle possessed of individual motive power, this corpuscle could go by many routes from the occipital lobe to the frontal." Indeed, because of the many vascular bridges across the midline, it could go from one hemisphere into the other. Therefore, "If one will hold to the theory of end-arteries in the brain, there is but one such vessel—the aorta!"

The work also shows that, for the cat at least, there is no anatomic distinction between arteries to the cortex and those to the underlying white matter. In fact, most arteries supply both. All enter from the pial surface, and most of the venous return comes through veins which flow outward from the deep capillary nets to the pial surface again. A smaller number of veins flow away along the white matter to join the deep cerebral veins, thus giving a certain amount of true through-and-through circulation to the cortex.

The circulation in the pia is described in detail; the author believes that he can divide it into three layers. The most external is the layer of pial arteries; these form anastomoses freely with one another. Beneath this lies the "venose Zwischennetz"; this is a layer of veins that has so much anastomosis that it resembles a spider's web. Between these two layers there are many arterio-venous anastomoses; so the blood must be mixed. Beneath these layers and really not lying in the pia, but apparently in the arachnoid space and on the brain surface, is a filigree-work of capillaries, which enters the outer cortical layer and runs across to the pial veins. This last layer therefore is loosely knit, with much space in three dimensions.

Pfeifer speaks of the angio-architecture of the cerebral cortex as the main point of his work. He shows that the arrangement of vessels in Ammon's horn is unique and bears a relationship to cellular architecture. He also shows pictures of the inferior olives and other nuclei in the bulb, which illustrate his point that where cells are numerous, the blood supply is rich. In the occipital lobe (figure 68) an especially rich capillary network is shown extending through the deeper layers of the area praeparietalis. In figures 69, 70 and 71 a similar capillary increase is shown in the area striata. He says: "The vessels of the cerebral cortex are

arranged architecturally both in relation to the cortical areas and the cortical layers." This part of the work is suggestive and interesting, but only twenty-one pages are devoted to the subject. The figures are not convincing and the evidence presented is insufficient. To prove that the angio-architecture corresponds to the cyto-architecture and myelo-architecture, one should use serial sections, appropriately stained. Here sections that are far from serial are used for comparison and they may even be from different animals altogether (e. g., compare figure 83 with figure 84, or figure 77 with figure 78). In figure 93, where the cells are stained in a section of injected brain, the result is too muddled to prove much. More work is needed in this field to convince investigators of the true relationship between cyto-architecture, myelo-architecture and angio-architecture. It is to be deplored that the author considers this his central problem and named the book "Angioarchitektionik der Grosshirnrinde," for his most beautiful and convincing work has to do with the general arrangement of the finer vessels in the cerebrum, cerebellum, medulla oblongata and pia-arachnoid.

The most surprising thing about the book, however, is that no description is given of the method of injection. There is nothing but one short paragraph in which it is casually mentioned that one can use "Carminleim," gelatin or ink. Nothing is said about the pressure used to inject the vessels, but the reader gets the impression from various places in the text that the injections are made with a syringe, at high pressure, and that it is an art to do it just right. The reader does not even know whether the beautiful photographs he is looking at are of vessels filled with India ink or colored gelatin. This is not the proper way for a scientist to publish a serious and important monograph of 157 pages.

One should not belittle the real importance of this work by trivial criticism; what can be considered the chief errors have just been mentioned. The critical attitude of the author toward the work of others, however, is somewhat annoying, especially when he takes so much credit to himself by such statements as "Ich in der Literatur wohl noch keinen Vorgänger habe." It would seem that Craigie and Lorreto de No should be given more credit, and the work of such finely disciplined men as Brodmann, Vogt and Economo should not be slightly alluded to as "eine Felderung nach rein subjektivem Ermessen" (p. 105). The author has made a distinct advance in the critical study of cerebral circulation; he has presented good evidence that "end-arteries" are never present in the brain, and that there is no distinction between "Rindenarterien" and "Markarterien." He has described the cerebral and pial circulation as a virtually continuous net with innumerable anastomoses. Moreover, he has described a new method for reproducing photographs of thick sections with a deep focus; this gives an astonishingly plastic impression, and the reproductions are beautiful. Realizing all these laudable achievements the reader is, nevertheless, troubled by the faults in presentation, and if one is physiologically trained many of the deductions as to function, drawn from anatomic observations, seem dangerous.

MONGOLISM. A STUDY OF THE PHYSICAL AND MENTAL CHARACTERISTICS OF MONGOLIAN IMBECILES. By KATE BROUSSEAU. Revised by H. G. Brainerd. Cloth. Price, $4.50. Pp. 210, with illustrations. Baltimore: Williams & Wilkins Company, 1928.

On account of the many striking physical anomalies and their implications concerning possible etiologic factors, mongolian imbecility always has been one of the most interesting forms of primary amentia. The authors have made a distinct contribution by bringing together all the known facts gathered from a comprehensive review of the literature and from a study of a series of personally observed cases.

After a consideration of the historical aspect and the relation of mongolism to race, sex, geographical distribution, etc., the authors discuss fully the etiology. Although the exact causative factors are unknown, they consider that the condition is not due to a reversion to a primitive mongolian type, to parental alcoholism, tuberculosis or syphilis (although these may be contributory factors), to neuropathic

heredity, to the extremes of life in one or both parents, to mental strain, to disease of the female reproductive organs, or to undernourishment or overwork of the mother, and that it has no relation to the order of birth or the number of children in the family — it may be possibly the result of some obscure disturbance of the ductless gland system, since every case shows some signs of such an imbalance.

The pathologic and physical characteristics, particularly the anatomic anomalies, are discussed at length. There are no abnormalities peculiar to mongolism; it is rather the combination of several that distinguishes the type. Anomalies of the eye are rarely lacking; the head is usually microbrachycephalic; the ears are malformed; the tongue is fissured and presents hypertrophic papillae; congenital heart defects are common; the genitalia are poorly developed, and the hands are stubby, the thumb and little finger being extremely short. There is no constant pathologic lesion of the ductless glands.

There are no characteristic sensory, motor or mental defects. Grave sensory disorders are rare — the deficiency in sensation probably being due to imperfect development of the higher centers. Hypotonia and poor coordination are frequent.

Mental peculiarities are not so noticeable as are the physical anomalies. With few exceptions mongols are placid, affectionate, good humored and fond of music and rhythm. The intelligence varies from idiocy to feeblemindedness, although the majority of patients are imbecile. The lag in mental development becomes more noticeable as the child grows older.

On account of the superficial resemblance between mongolism, sporadic cretinism, achondroplasia and rachitis, the differential diagnosis is discussed fully.

The prognosis for life is poor. Mongols are so delicate and have so little resistance against infectious diseases that they succumb frequently during the first few months of life; less than 60 per cent reach 5 years of age and few reach maturity. After adolescence those that survive age rapidly.

At present no specific treatment is known. Thyroid medication has produced a slight improvement in a few cases. Institutional care seems advisable because of the tendency of the parents to over-protect these children on account of their obvious defects. Pedagogic therapy, particularly training in sense discrimination, coordination and speech, is desirable, but should not include academic or trade education for which the mongol is unfit. Constant medical care is necessary because of the low vitality. (It seems unfortunate that in such an excellent presentation of therapeutic measures the authors should include the statement that bed-wetting is usually the result of inattention or sheer laziness and must be treated by disciplinary measures.)

An appendix contains an abstract of twelve cases personally studied.

The comprehensive material is well arranged and is supplemented by numerous tables, good illustrations and an apparently complete bibliography. The book is a valuable survey of what is known at present concerning mongolism.

INFANCY AND HUMAN GROWTH. By ARNOLD GESELL. Price, $3.50. Pp. 410, with illustrations. New York: The Macmillan Company, 1928.

This book is a continuation of the studies initiated by Gesell in his previous book, "The Mental Growth of the Pre-School Child." It contains a great deal of material on the growth of the infant. Gesell makes use of the comparative study of infants, a method which he stressed in his first book. By this means the author is able to observe, by contrast, characteristics which would otherwise escape attention. He was able to make studies of infants at various age levels, observing those with a difference in age of exactly one month. It is difficult to accept the fact that what is true of one child of 1 month or 6 months of age is necessarily true of all children of these ages. Yet on this basis of individual studies at various age levels Gesell says that there are certain basic uniformities in the dynamics of development which apply to all infants, normal, abnormal, superior and inferior. There is a large system of uniformities which characterize all normal infants and keep them traveling on highly similar routes and on highly similar

timetables. A large part of the first portion of the book is taken up with a description of the methods used in the observation of the infants studied. One of the valuable portions of the book consists in a graded schedule of the various performances to be expected of a child at various stages of its development. These include motor and language development, adaptive behavior and personal-social behavior. They are based apparently on a large series of observations, though the exact number is not stated. Normative summaries are presented for infants 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 18, 21, 24 and 30 months of age.

The second part of the book is given to a discussion of the tempo and trend of infant development. Gesell states that "mental growth is conceived as a process or complex, ordered and conditioned by the factor of age. This process as an organic whole has a characteristic rate of progression (tempo). It has a general trend indicated by its past and potential products. It has personal pattern determined by the configuration and dynamic interplay of its components."

Gesell draws few conclusions on the basis of his studies. This, however, may merely serve to emphasize the fact that the field of psychologic studies of infants is still in an early stage of development. Much more material based on the study of many cases is needed to make the studies conclusive. There is an interesting chapter on the growth of the premature infant. Gesell concludes that "the maturation of early behavior tends to follow an inherent genetic order irrespective of the time of birth." He tends to straddle the question of the influence of heredity and environment.

NEUROLOGISCHE WANDTAFELN. Compiled by FRIEDRICH MÜLLER, FRIEDRICH HILLER and HUGO SPATZ (Second series). Price, 100 m, with 10 charts. Munich: J. F. Lohmanns.

This second series of the neurologic charts or wall tables completes the series. The first ten tables, which were reviewed in a previous issue, showed mainly the representation of the brain. This second series consists of ten tables and shows the following: a schematic representation of the motor and sensory fibers; the segmental skin representation; the peripheral nerve representation; the arteries of the brain; the visual projection system in its entirety; the spinal segments in relation to the vertebrae, showing at the same time the muscles and reflex centers; the cell and myelin architecture of the cerebrum; the intra-uterine development of the brain; the myelin development of the brain and cord in a new-born infant, and the sympathetic innervation of the neck, chest and abdomen.

It would be impossible to overestimate the value of these charts from a teaching standpoint. They make teaching easier. They are clearcut and large enough so that they can be well seen by the average student away from the lecturer. They stand out because of the contrasting colors used, and are sufficiently well marked so that there is no question in the mind of the observer as to what he is seeing.

As was stated in the review of the first series, they are beautiful, and no laboratory or teacher can afford to do without them.

A LABORATORY AID FOR THE STUDY OF NEURO-ANATOMY. By J. H. GLOBUS, M.D. Price, $3. Pp. 68. New York: Paul B. Hoeber, 1928.

This little laboratory guide is an effort on the part of the author to revise the methods of study of the anatomy of the nervous system. As a result, he has prepared outlines of various levels of the nervous system which the student is supposed to fill in and label. The first drawing of the series is completely filled out and labeled so that it may serve as a guide to the treatment of the remaining outlines. The whole plan is ingeniously developed. A suggestion is made that the student select a different color for different tracts, but that he maintain each tract in the same color no matter where found, thus tending to easy identification. The author has shown good judgment in his selection of the various levels. Teachers of neuro-anatomy will do well to consider this book and its suggestions.

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